Archives of Neurology and Psychiatry

VOLUME 57 FEBRUARY 1947 NUMBER 2



# VOLUME FLOW OF BLOOD THROUGH THE HUMAN BRAIN

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VALID quantitative data on the volume flow of blood through the human brain are of crucial importance for the solution of a variety of clinical and theoretic problems. The poverty of such data has been due chiefly to a lack of suitable technics. The thermoelectric flow recorder devised by one of us (F. A. G) [1] does not yield qualitative data unless calibrated in situ, and this has not been done in man. Ferris [2] has employed a method by which the bone-supported dural coverings of the brain and spinal cord are used as a plethysmograph. A trochar is inserted into the lumbar sac, and with an inflatable cuff the veins of the neck are compressed. The cerebral blood flow is estimated from the rate of displacement of spinal fluid. Kety and Schmidt [3] have recently described a method based on the principle that the rate at which the brain comes into equilibrium with the concentration of a physiologically inert and freely diffusible substance is a function of the cerebral blood flow; this rate is determined by plotting against time the difference in concentration of the substance in the arterial and the cerebral venous blood. Comments on the methods of Ferris and of Kety and Schmidt and comparison of their results with those of the present study will be found in the succeeding paragraphs.

## METHOD

By injecting at constant rate a physiologically inert, nondiffusible substance into a major cerebral artery and then determining the concentration of that substance in a major cerebral venous channel, it is possible to estimate the

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1. Gibbs, F. A.: A Thermoelectric Blood Flow Recorder in the Form of a Needle, Proc. Soc. Exper. Biol. & Med. **31**:141-146, 1933.

2. Ferris, E. B.: Objective Measurement of Relative Intracranial Blood Flow in Man, Arch. Neurol. & Psychiat. **46**:377-401 (Sept.) 1941.

3. Kety, S. S., and Schmidt, C. F.: The Determination of Cerebral Blood Flow in Man by the Use of Nitrous Oxide in Low Concentrations, Am. J. Physiol. **143**:53-66, 1945.

volume flow of blood through the brain (F. A. G.). If mixing is complete, the ratio of the concentration of the injected substance to its concentration in the sample of blood from the major venous channel will be inversely proportional to the ratio of the rate of injection to the rate of blood flow; i. e., the dilution factor times the rate of injection equals the minute-volume flow of blood through the brain. However, when the period of injection has continued beyond the circulation time, some of the injected substance will reach the general arterial stream, and this will require that the concentration of the substance in the general arterial stream be subtracted from the concentration in the cerebral venous sample.

The substance chosen for injection in the present study was Evans blue (T-1824). It was injected into the right internal carotid artery by means of a constant speed injection apparatus of the type described by Koehler.[4] The original plan had been to inject the dye and withdraw samples through indwelling needles inserted through the previously unbroken skin, but it was decided that for preliminary studies it would be wiser to cut down on the great vessels of the neck, thus guarding against possible extravasation of the dye or failure because of inability to puncture the correct vessels.

## MATERIAL

Since an open operation was decided on, only special types of patients could be used. The first 2 had inoperable gliomas; the third was a psychopathic patient who craved operation; the fourth was a patient with convulsions and right hemiplegia; the fifth had severe unilateral paralysis agitans, and the sixth had advanced progressive muscular atrophy without any known intracranial pathologic condition. The seventh patient had alcoholic encephalitis. Probably because of the dramatic value of the surgical procedure, the increased attention from physicians and the greater nursing care, all patients reported that they felt better after the operation.

## OPERATIVE PROCEDURE

With local anesthesia, the bifurcation of the right common carotid artery and the right internal jugular vein with its local branches was exposed. A large ureteral catheter was then introduced through a branch of the jugular vein up to the level of the jugular bulb. A no. 22 intravenous needle, through which the dye was injected, was then introduced into the lumen of the internal carotid artery.

When the volume of cerebral blood flow was measured directly, both sides were exposed and a heavy loop of black silk was placed high in the neck around the left internal jugular vein. The ends of the silk loop were threaded through a large silk-woven catheter, so that the blood flow through the left internal jugular vein could be stopped by placing tension on the silk loop. On the right side a large rubber cannula was inserted into the right internal jugular vein after all the local branches had been ligated and divided. Thus, the cerebral venous return could be entirely deflected through the right internal jugular vein during temporary occlusion of the left internal jugular vein.

## INJECTION AND SAMPLING

The syringe on the constant speed injector was filled with an 0.2 per cent solution of Evans blue. The motor was then started, providing a flow

4. Koehler, A. E.: A Simplified Apparatus for Constant Rate Injections, J. Lab. & Clin. Med. **26**:383-385, 1940.

of 1 cc. per minute of the dye solution into the internal carotid artery. After allowing at least two minutes for equilibrium to be established between the dye stream and the blood stream, a 10 cc. sample was drawn from the catheterized jugular bulb; this sample was discarded and a second 10 cc. sample drawn, which was retained. Simultaneously with drawing of the second sample from the jugular bulb, a 10 cc. sample was drawn from the left femoral artery. Thereafter, heparin was injected into the jugular catheter to prevent clotting, and a stylet was inserted into the femoral needle for the same purpose. This sampling procedure was repeated whenever an estimate of cerebral blood flow was desired.

The concentration of dye in the arterial and the venous samples was determined by photoelectric colorimetry. Six cubic centimeter samples of blood were centrifuged, and the concentration of the dye in the plasma was determined. If hemolysis was present, a correction was applied by using a formula provided by Gibson and Evelyn.[5] The ratio of plasma to cells was determined with the hematocrit, and the amount of dye in the whole blood was calculated from another of Gibson's formulas.[5] The minute volume flow of blood through the brain was determined as follows:

$$\frac{\text{Concentration of dye injected}}{\text{Concentration of dye in internal jugular vein} - \text{concentration of dye in artery}} \times \text{cc. dye injected per min.} = \text{blood flow (cc./min.)}$$

The oxygen and carbon dioxide contents of all samples of blood were determined by the Van Slyke manometric method,[6] and sugar values, by the Nelson adaptation of the Somogyi method.[7] Arteriovenous differences for oxygen, sugar and carbon dioxide multiplied by minute volume flow gave values for the oxygen and sugar consumption of the brain and its production of carbon dioxide. Attempts were made to alter the cerebral blood flow by having the patient hyperventilate and by adding 5 or 10 per cent carbon dioxide to the respired air.

## SOURCES OF ERROR

The chief source of error is failure of the dye to mix completely with the total cerebral venous blood. If part of the dye reaches a channel that by-passes the internal jugular veins, the concentration in the internal jugular vein will be too low and the calculated flow will be erroneously high. If the stream in the right internal carotid artery leads into relatively isolated venous channels, where it is unmixed with blood from all other cerebral arteries, and the dye is thus carried in high concentration to the right internal jugular vein, an erroneously low value for cerebral blood flow will be obtained.

It is customary, when expressing the results of in vitro studies with the Warburg apparatus, to give the oxygen consumption in terms of cubic centimeters of oxygen per gram (or 100 Gm.) of dry brain. A distinction also is made between the oxygen consumption of gray matter and that of white matter.

5. Gibson, J. R., Jr., and Evelyn, K. A.: Clinical Studies of Blood Volume: IV. Adaptation of Method to Photoelectric Microcolorimeter, J. Clin. Investigation **17**:153-158, 1938.

6. Van Slyke, D. D., and Neill, J. M.: The Determination of Gases in Blood and Other Solutions by Vacuum Extraction and Manometric Measurement, J. Biol. Chem. **61**:523-573, 1924.

7. Nelson, N.: A Photometric Adaptation of the Somogyi Method for the Determination of Glucose, J. Biol. Chem. **153**:375-380, 1944.

Such precision is difficult, if not impossible, to obtain in vivo. In the present study no information is available as to the weight of the brain, nor is it known what part of the flow from the cerebellum and the hindbrain is included.

It must be realized that as flow increases arteriovenous differences of oxygen content and of dye concentration both approach zero and both become relatively insensitive indicators of flow. Consequently, an over-all percentage accuracy would be meaningless, and the same holds for the needle flow recorder.[1] A quantitative check against direct volumetric determinations was carried out in 1 case; this is referred to in the next section.

Two of the patients had large intracranial tumors which might have been expected to alter cerebral blood flow. The patient with seizures and hemiplegia must have had some cerebral atrophy. Only 2 of the patients (cases 3 and 6, in table 2) can be presumed to have had normal brains.

## RESULTS

Table 1 shows the values for three direct volumetric determinations of cerebral blood flow in 1 case, together with the values obtained

TABLE 1.—*Data for Cerebral Blood Flow by Direct Volumetric and Dye Injection Methods and Arteriovenous Differences in Oxygen, Carbon Dioxide and Glucose*

| Procedure | Cerebral Blood Flow | | Arteriovenous Differences | | |
|---|---|---|---|---|---|
| | Direct Volumetric Method, Cc./Min. | Dye Injection Method, Cc./Min. | Oxygen, Vol. % | Carbon Dioxide, Vol. % | Glucose, Mg./100 Cc. |
| Room air | 370 | 378 | 7.14 | 7.35 | 10 |
| Low carbon dioxide | 320 | 327 | 9.89 | 10.04 | 15 |
| High carbon dioxide | 348 | 401 | 5.79 | 5.51 | 11 |

with the dye injection technic, and also arteriovenous differences for oxygen, carbon dioxide and glucose. In two of these determinations the data for the dye injection method and the direct volumetric method agreed to within 3 per cent and the change in arteriovenous difference for oxygen was entirely consistent with the change in blood flow.

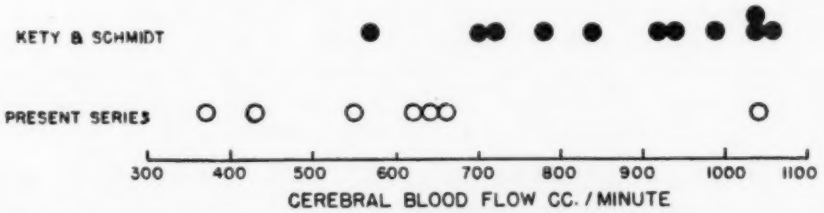


Fig. 1.—Distribution of values for minute blood flow through the brain in the present series of 7 cases and in the series reported by Kety and Schmidt.[3]

In the third, the dye injection method gave values for the cerebral blood flow in accord with the change in the arteriovenous difference for oxygen, but the volumetric determination of flow gave data at variance.

This discrepancy is believed to have been due to an error in technic, probably a failure to occlude completely the left internal jugular vein during the time that the flow from the right internal jugular vein was being collected.

The oxygen, carbon dioxide and sugar contents of the arterial and the internal jugular blood, the arteriovenous differences and the cerebral blood flow and oxygen consumption during rest, hyperventila-

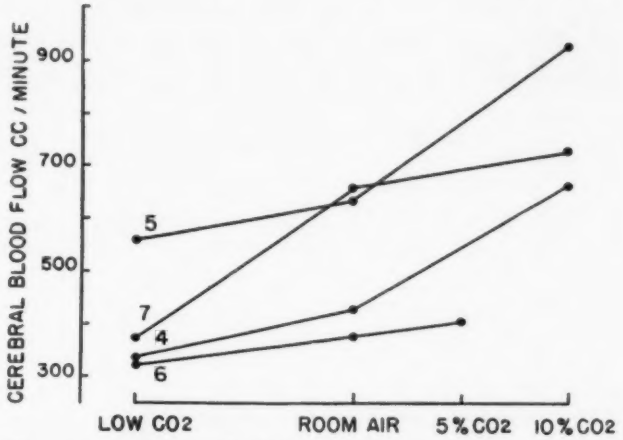


Fig. 2.—Changes in the cerebral blood flow occurring in 4 cases in which both higher and lower concentrations of carbon dioxide were breathed.

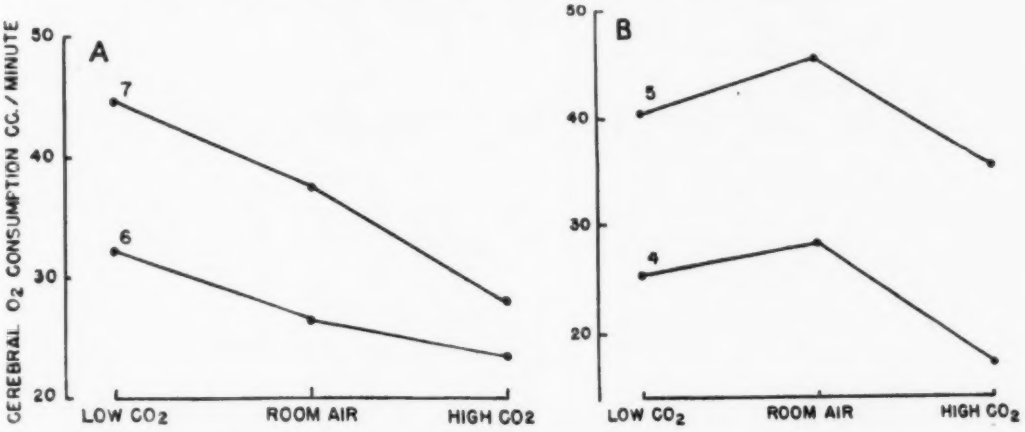


Fig. 3.—Changes in oxygen consumption with hyperventilation in the 4 cases values for which are shown in figure 3.

tion and breathing of high carbon dioxide mixtures are shown in table 2. Figure 1 shows the distribution of values for minute volume flow of blood through the brain as determined by us and the values reported for their cases by Kety and Schmidt.[3]

In all the present cases in which hyperventilation was employed, the cerebral blood flow decreased; in all cases in which carbon dioxide was

TABLE 2.—*Data on Oxygen, Carbon Dioxide and Glucose Contents of Arterial and Internal Jugular Venous Blood and on Oxygen Consumption and Blood Flow of the Brain*

| Case No. | Procedure | Oxygen Content, Vol. % | | Carbon Dioxide Content, Vol. % | | Glucose, Mg./100 Cc. | | Arteriovenous Difference | | | Oxygen Uptake, Cc./Min. | | Blood Flow, Cc./Min.: |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Arterial | Internal Jugular | Arterial | Internal Jugular | Arterial | Internal Jugular | Oxygen, Vol. % | Carbon Dioxide, Vol. % | Glucose, Mg./100 Cc. | Whole Brain | 100 Gm. of Brain | Whole Brain |
| 1 | Room air | 19.56 | 11.98 | 48.62 | 55.97 | 138 | 125 | 7.58 | 7.35 | 13 | 41.5 | 2.9 | 548 |
| | Low carbon dioxide | ..... | ..... | ..... | ..... | ... | ... | .... | .... | .. | .... | ... | ... |
| | High carbon dioxide | 20.52 | 15.92 | 50.90 | 55.09 | 134 | 127 | 4.60 | 4.19 | 7 | 27.8 | 2.0 | 606 |
| 2 | Room air | 18.73 | 13.81 | 48.81 | 53.73 | 93 | 85 | 4.92 | 4.92 | 8 | 30.3 | 2.2 | 619 |
| | Low carbon dioxide | ..... | ..... | ..... | ..... | ... | ... | .... | .... | .. | .... | ... | ... |
| | High carbon dioxide | 19.87 | 18.73 | 57.30 | 58.47 | 90 | 87 | 1.14 | 1.17 | 3 | 14.9 | 1.1 | 1,304 |
| 3 | Room air | 21.90 | 15.72 | 44.48 | 50.80 | 142 | 134 | 6.18 | 6.32 | 8 | 64.4 | 4.6 | 1,039 |
| | Low carbon dioxide | 22.65 | 9.68 | 37.96 | 50.80 | 148 | 127 | 12.97 | 12.84 | 21 | 44.8 | 3.2 | 353 |
| | High carbon dioxide | ..... | ..... | ..... | ..... | ... | ... | .... | .... | .. | .... | ... | ... |
| 4 | Room air | 19.26 | 12.73 | 47.06 | 53.43 | 92 | 83 | 6.53 | 6.37 | 9 | 28.1 | 2.0 | 433 |
| | Low carbon dioxide | 19.32 | 11.77 | 38.35 | 48.93 | 92 | 81 | 7.55 | 10.58 | 11 | 25.6 | 1.8 | 337 |
| | High carbon dioxide | 19.72 | 17.14 | 51.85 | 53.93 | 91 | 86 | 2.58 | 2.08 | 5 | 17.3 | 1.2 | 666 |
| 5 | Room air | 19.68 | 12.55 | 43.43 | 50.45 | 111 | 100 | 7.13 | 7.02 | 11 | 45.5 | 3.3 | 641 |
| | Low carbon dioxide | 19.68 | 12.43 | 43.44 | 50.48 | 107 | 98 | 7.25 | 7.04 | 9 | 40.5 | 2.9 | 563 |
| | High carbon dioxide | 21.02 | 17.21 | 46.24 | 50.10 | 107 | 102 | 3.81 | 3.86 | 5 | 35.4 | 2.5 | 932 |
| 6 | Room air | 20.76 | 13.62 | 47.01 | 54.36 | 99 | 89 | 7.14 | 7.35 | 10 | 26.6 | 1.9 | 378 |
| | Low carbon dioxide | 22.19 | 12.30 | 44.22 | 54.26 | 103 | 88 | 9.89 | 10.04 | 15 | 32.2 | 2.3 | 327 |
| | High carbon dioxide | 22.67 | 16.88 | 49.14 | 54.65 | 104 | 93 | 5.79 | 5.51 | 11 | 23.8 | 1.7 | 401 |
| 7 | Room air | 20.20 | 14.52 | 41.21 | 46.69 | 140 | 133 | 5.68 | 5.48 | 7 | 37.8 | 2.7 | 662 |
| | Low carbon dioxide | 22.08 | 9.69 | 31.90 | 44.84 | 139 | 127 | 12.39 | 12.94 | 12 | 44.8 | 3.2 | 370 |
| | High carbon dioxide | 23.08 | 19.50 | 44.71 | 46.83 | 143 | 136 | 3.58 | 2.12 | 7 | 28.0 | 2.0 | 732 |

breathed, the cerebral blood flow increased (table 2). The changes in cerebral blood flow that occurred in the 4 cases in which carbon dioxide was both lowered and raised are shown in figure 2.

Calculations of oxygen uptake based on cerebral blood flow and arteriovenous differences in oxygen indicate that the oxygen uptake was reduced in all cases in which carbon dioxide was increased (table 2). However, no such consistency was found with hyperventilation; in 3 cases the oxygen uptake was decreased, and in 2 it was increased (table 2). In figure 3 *A* and *B* are shown the changes in oxygen uptake in the 4 cases in which carbon dioxide was both lowered and raised.

## COMMENT

The values obtained for cerebral blood flow in the present study are approximately three times as great as those of Ferris.[2] They are in general lower than, but in fairly close accord with, the values reported by Kety and Schmidt.[3] If the present values for cerebral blood flow are used for calculating oxygen consumption per gram of brain (assuming a brain weight of 1,400 Gm.), values are obtained having the same order of magnitude as the initial rate of oxygen consumption for brain in vitro.[8] The results are also in general accord with the values for cerebral oxygen consumption obtained from in vivo studies on monkeys by Schmidt, Kety and Pennes.[9]

The present findings prove conclusively that lowering the carbon dioxide level of arterial blood causes a decrease in cerebral blood flow, and raising it causes an increase. This conclusion is supported by previous evidence based on the caliber of cerebral vessels[10] and by qualitative changes in cerebral blood flow as measured either with a needle flow recorder[1] or by Ferris' spinal fluid displacement method.[2] They are also in accord with amperemetric determinations of cerebral oxygen tension as reported by Roseman, Goodwin and McCulloch.[11]

Lennox and 2 of us (F. A. G. and E. L. G.)[12] have shown that at normal oxygen levels carbon dioxide is more effective than oxygen in altering cerebral arteriovenous differences. However, at low levels

8. Warburg, O.; Posener, K., and Negglein, E.: Ueber den Stoffwechsel der Carcinomzelle, Biochem. Ztschr. **152**:309-344, 1924.

9. Schmidt, C. F.; Kety, S. S., and Pennes, H. H.: The Gaseous Metabolism of the Brain of the Monkey, Am. J. Physiol. **143**:33-52, 1945.

10. Wolff, H. G., and Lennox, W. G.: Cerebral Circulation: XII. The Effect on Pial Vessels of Variations in the Oxygen and Carbon Dioxide Content of the Blood, Arch. Neurol. & Psychiat. **23**:1097-1120 (June) 1930.

11. Roseman, E.; Goodwin, C. W., and McCulloch, W. S.: Rapid Changes in Cerebral Oxygen Tension Induced by Altering the Oxygenation and Circulation of the Blood, J. Neurophysiol. **9**:33-40, 1946.

*(Footnotes continued on next page)*

the situation is reversed: Carbon dioxide produces little change, and oxygen produces great changes. Under conditions of relative anoxia, therefore, a close relationship is found in the arteriovenous differences, the oxygen level and cerebral metabolism. In our opinion, homeostasis for oxygen is an emergency mechanism that does not appear until the oxygen supply to the brain is threatened. At normal oxygen levels the cerebral blood flow is regulated to give a homeostasis for carbon dioxide. The arterial oxygen content in many of the cases reported by Schmidt, Kety and Pennes[9] suggests that they were working in a low oxygen zone, where carbon dioxide is ineffective as a determinant of cerebral blood flow and where the oxygen level and the oxygen requirement, and therefore the metabolism, are the predominant determinants.

Under the conditions of the present experiments, an increase in cerebral blood flow (produced with high carbon dioxide levels) was associated with a decrease in cerebral oxygen uptake. The antianoxic action of carbon dioxide has been recognized for a long time. It has been suspected that this action was due in part to a direct depressant action of carbon dioxide on cerebral oxygen uptake. The data obtained in the present study are in accord with such an assumption.

## SUMMARY

By means of a dye injection method, which in 1 instance was checked against direct volumetric determinations, the cerebral blood flow of man was measured in 7 patients. The average resting flow for all subjects was 617 cc. per minute.

By hyperventilation it was possible to reduce the cerebral blood flow approximately one-half. By breathing 10 per cent carbon dioxide, it was possible to double the cerebral blood flow. Under the conditions of these experiments, the major changes which occur in arteriovenous differences of oxygen are the result of change in the cerebral blood flow. However, in all cases the oxygen uptake of the brain was reduced by high carbon dioxide concentrations; no consistent change in oxygen uptake occurred with hyperventilation.

University of Illinois School of Medicine.

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12. Lennox, W. G.; Gibbs, F. A., and Gibbs, E. L.: The Relationship in Man of Cerebral Activity to Blood Flow and to Blood Constituents, J. Neurol. & Psychiat. **1**:210-225, 1938. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: The Value of Carbon Dioxide in Counteracting the Effects of Low Oxygen. Aviation Med. **14**:1-2, 1943.

# RELATION OF ACUTE MUCOSAL HEMORRHAGES AND ULCERS OF GASTROINTESTINAL TRACT TO INTRACRANIAL LESIONS

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CUSHING, in his Balfour Lecture,[1] stated that erosions and ulcers in the gastrointestinal tract are not infrequently seen in association with various cerebral lesions and after intracranial operations. He reviewed the literature covering this subject up to 1932. The generally accepted opinion is that these ulcers follow certain intracranial processes which cause a state of parasympathetic irritation or sympathetic paralysis of autonomic centers in the hypothalamus. A number of experimental studies were dedicated to this problem.[2] Mechanical or chemical stim-

From the Laboratory of the Metropolitan State Hospital.

1. Cushing, H.: Peptic Ulcer and the Interbrain (Balfour Lecture), Surg., Gynec. & Obst. **55**:1 (July) 1932.

2. Durante, L.: The Trophic Element in Origin of Gastric Ulcers, Surg., Gynec. & Obst. **22**:399, 1916. Gundelfinger, E.: Klinische und experimentelle Untersuchungen über den Einfluss des Nervensystems bei der Entstehung des runden Magengeschwürs, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **30**:189, 1918. Berg, M.: Experimental Peptic Ulcer by Vasomotor Episodes (Pitressin Episodes) and Autonomic Disturbances, Arch. Path. **33**:636 (May) 1942. Beattie, J.: Relation of Tuber Cinereum to Gastric and Cardiac Functions, Canad. M. A. J. **26**:278 (March) 1932; Hypothalamic Mechanisms, ibid. **26**:400 (April) 1932. Burdenko, N., and Mogilnitzky, B. N.: Zur Pathogenese einiger Formen des runden Magengeschwürs, Ztschr. f. d. ges. Neurol. u. Psychiat. **103**:42, 1926. Mogilnitzky, B. N.: Zur Frage der Entstehungsweise und Ursache neurogener Formen des runden Magengeschwürs, Virchows Arch. f. path. Anat. **257**:109, 1925. Keller, A.: Ulceration of the Digestive Tract in the Dog Following Intracranial Procedures, Arch. Path. **21**:127 (Feb.) 1936. Keller A.; Hare, D., and D'Amour, C.: Ulceration in Digestive Tract Following Experimental Lesions in Brain-Stem, Proc. Soc. Exper. Biol. & Med. **30**:772 (March) 1933. Keller, A., and D'Amour, C.: Ulceration in the Digestive Tract of Dog Following Hypophysectomy, Arch. Path. **21**:185 (Feb.) 1936. Watts, J., and Fulton, J.: The Effect of Lesions of the Hypothalamus upon the Gastro-Intestinal Tract and Heart of Monkeys, Ann. Surg. **101**:363 (Jan.) 1935. Light, R. U.; Bishop, C. C., and Kendall, L. G.: The Production of Gastric Lesions in Rabbits by Injection of Small Amounts of Pilocarpine into the Cerebrospinal Fluid, J. Pharmacol. & Exper. Therap. **45**:227 (June) 1932. Hoff, E., and Sheehan, D.: Experimental Gastric Erosions Following Hypothalamic Lesions in Monkeys, Am. J. Path. **11**:789 (Sept.) 1935. Nedzel, A. J.: Experimental Production of Gastric Ulcers in Dogs by Inducting Vascular Spasm with Pitressin, Am. J. Digest. Dis. **10**:283 (Aug.) 1943; Experimental Gastric Ulcer (Pitressin Episodes), Arch. Path. **26**:988 (Nov.) 1938.

ulation of the hypothalamic region was frequently followed by hemorrhages or erosions of the gastrointestinal tract. Since Cushing's paper, the coincidence of cerebral lesions and acute peptic ulcers in man has been reported only occasionally.[3] The purpose of the present paper is to elucidate as far as possible how frequently and under what conditions acute mucosal hemorrhages and erosions of the gastrointestinal tract may be observed with and without fatal intracranial lesions.

## MATERIAL

Available for this study were the large autopsy material of the Office of the Chief Medical Examiner of New York City (Dr. Thomas A. Gonzales) during a two year period (about 1,200 cases) and 196 cases in which autopsy was performed occurring during a similar period in two state hospitals for mental disease. These 196 cases with autopsy were divided into five groups. Group 1 consisted of 59 cases in which no hemorrhages, erosions or softenings of the gastrointestinal tract were observed at autopsy. Group 2 consisted of 89 cases in which autopsy showed mucosal hemorrhages of the stomach or duodenum (or in other parts of the intestine) without gross evidence of effusion of blood into the gastrointestinal tract. Group 3 consisted of 24 cases in which the mucosal hemorrhages had produced gross bleeding into the lumen of the stomach and/or the intestine. Group 4 consisted of 14 cases in which acute hemorrhagic ulcerations of the upper gastrointestinal tract were observed at autopsy. Group 5 consisted of 10 cases in which autopsy revealed advanced gastromalacia. The ages of the 196 patients varied from 16 to 94 years, and the cases were distributed equally between the sexes. The psychosis and the terminal disease were of very different types in all five groups. In group 4 were included also 12 cases of acute gastroduodenal ulcer, and in group 5, 30 cases of nontraumatic perforation of the esophagus or stomach, observed at and collected from about 1,200 autopsies performed by the Office of the Chief Medical Examiner of New York City.

## OBSERVATIONS

Group 1.—In 59 of 196 cases with autopsy (or 30.1 per cent) no mucosal hemorrhage of the gastrointestinal tract was observed. In this group only 3 cases of severe cerebrovascular lesions (thrombotic softenings) were encountered. The types of the psychosis and of the terminal illness varied widely in this group.

Group 2.—In 89 of 196 cases with autopsy (or 45.4 per cent) more or less numerous mucosal hemorrhages were observed in the stomach or duodenum, frequently associated with hemorrhages in other parts of the intestine. The hemorrhages varied from a few small ecchymoses in the fundus of the stomach to numerous linear hemorrhages involving large parts of the stomach and duodenum. The cause and mechanism of death in this group were also variable. There were 6 cases of a severe cerebral lesion in this group (2 of spontaneous cerebral hemorrhage, 2 of large cerebral thromboses, 1 of cerebral tumor [ependymoma] and

3. Masten, M., and Bunts, R. C.: Neurogenic Erosions and Perforations of the Stomach and Esophagus in Cerebral Lesions: Report of Six Cases, Arch. Int. Med. **54**:916 (Dec.) 1934.

1 of cerebral abscess). The gross and microscopic pictures of the mucosal hemorrhages in the 6 cases were not different from those observed in cases without cerebral lesions.

Histologically, there were superficial necrosis, edema and extravasation of red cells into the mucosa. As a rule the mucosal and submucosal vessels in the hemorrhagic area were engorged with red cells.

GROUP 3.—In 24 of 196 cases (or 12.3 per cent) mucosal hemorrhages of the stomach or duodenum, with dark brownish fluid in the stomach and tarry stools, were observed at autopsy. Cases of bleeding from peptic ulcer, tumor or inflammatory processes of the gastrointestinal tract were excluded from this group. In 5 cases, however, local circulatory disturbances could have caused the bleeding into the stomach

Fig. 1 (case 1).—Lower portions of the esophagus of a woman aged 78, who had a psychosis with cerebral arteriosclerosis. Multiple circular hemorrhagic ulcers, with blackish borders, and bleeding into the gastrointestinal tract were present.

or intestine. These were 2 cases of cirrhosis of the liver, 1 case of volvulus of the sigmoid and 2 cases of myocardial failure from hypertensive heart disease. In 9 out of 24 cases there were gross intracranial lesions; these were 3 cases of spontaneous cerebral hemorrhages, 2 cases of laceration of the brain associated with subdural and subarachnoid hemorrhages, 1 case of cerebral tumor (meningioma), 1 case of dementia paralytica, 1 case of Alzheimer disease and 1 case of sudden death in the catatonic state with cerebral edema. The microscopic picture in the hemorrhagic area differed only slightly from that seen in group 2. Necrosis, edema and effusion of red cells into the mucosa were, however, more extensive, and there was a cellular reaction, con-

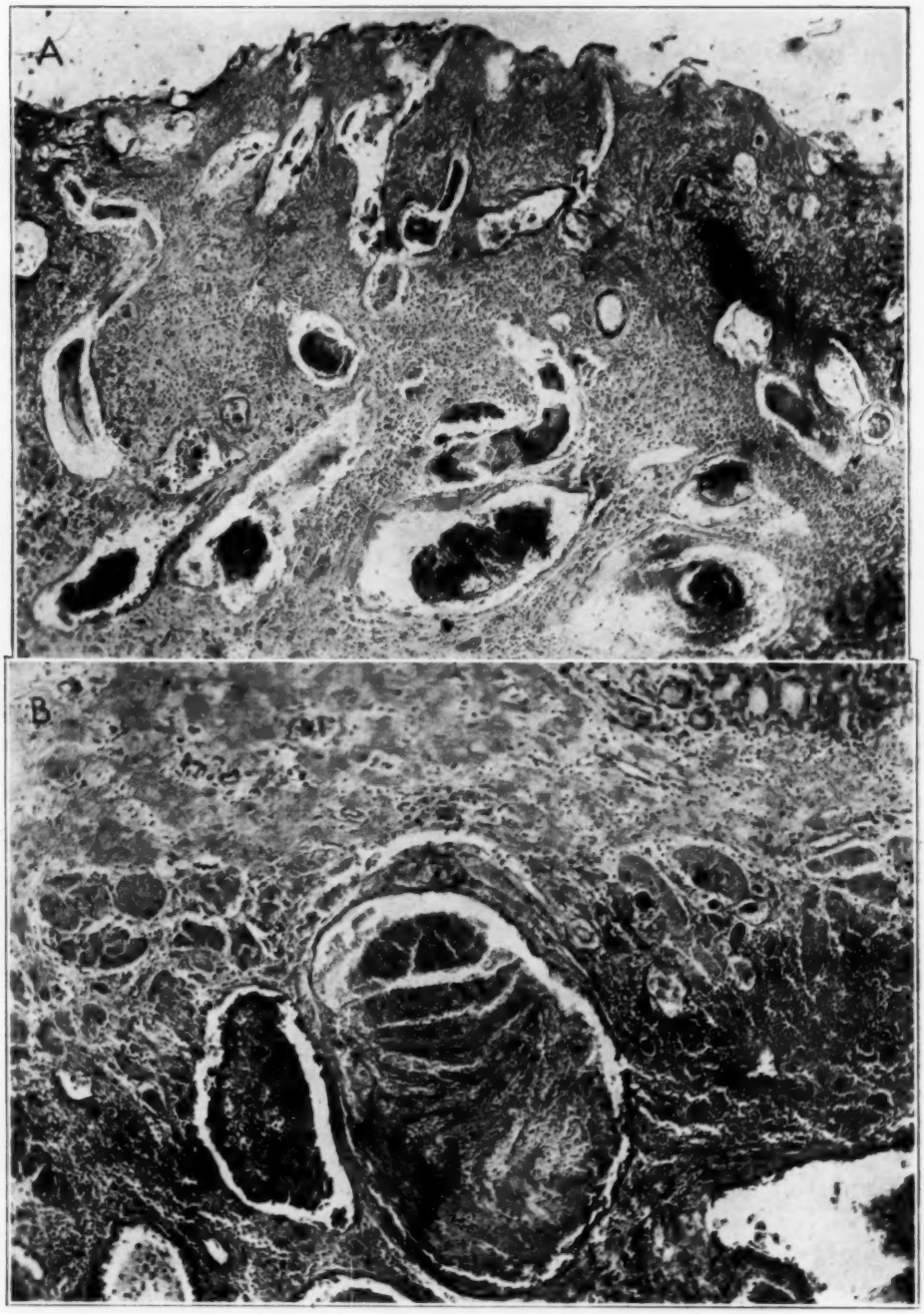
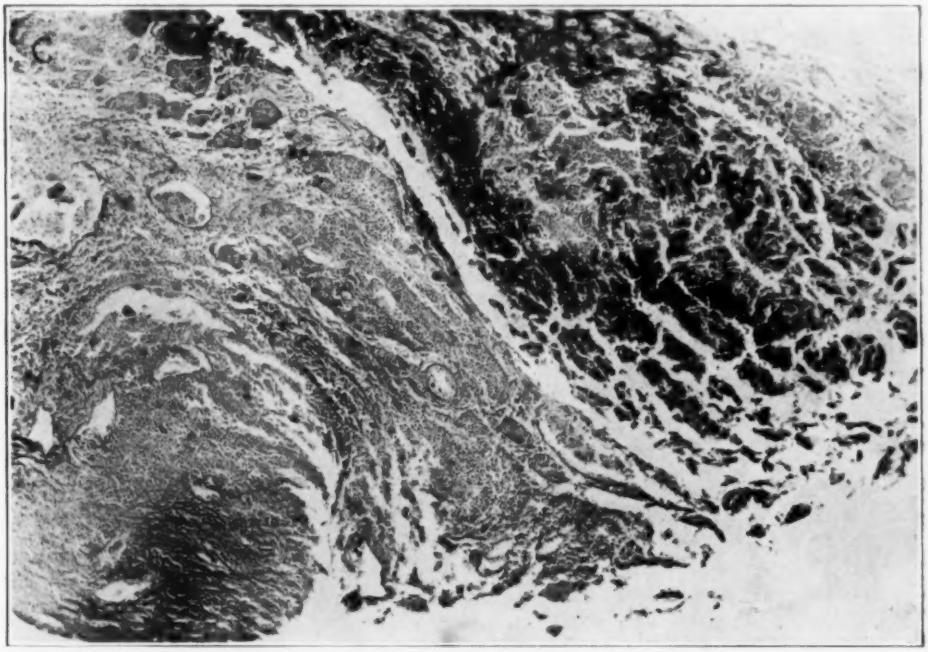



Fig. 2 (case 1).—*A*, area of esophageal ulcers, showing necrosis, edema, inflammatory reaction, engorged vessels and thrombi in mucosal and submucosal veins. Note diffuse blackish discoloration in the right corner due to hemorrhagic infiltration. Hematoxylin and eosin stain; × 45.

*B*, portion of the same area as that in *A*, showing large thrombus in a submucosal vein surrounded by cellular infiltrates, consisting mostly of polymorphonuclear leukocytes. Hematoxylin and eosin stain; × 84.

sisting in accumulations of polymorphonuclear leukocytes, which extended from the necrotic area of the mucosa into the submucosa. The mucosal and submucosal blood vessels were engorged with red cells.

GROUP 4.—In 14 of 196 cases (or 7.1 per cent) acute hemorrhagic ulcerations of the upper gastrointestinal tract were observed at autopsy. In 3 [4] of the 14 cases the ulcers were situated in the lower portion of the esophagus; in 5 cases, in the stomach (in the fundus near the cardia), and in 6 cases, in the upper portion of the duodenum. Of 12 additional cases of the same type observed at the Office of the Chief Medical Examiner of New York City, the ulcers were situated in the stomach



*C*, another part of the ulcer, showing edema, necrosis, cellular infiltration of the mucosa and submucosa and diffuse blackish discoloration of the superficial and deeper necrotic layers due to formation of hemosiderin (appearing black in the picture). Stain for hemosiderin; × 76.

in 6 cases and in the duodenum in 6 cases. Tarry stool or brownish fluid in the stomach was found in all 26 cases.

*Lower Portion of Esophagus.*—Acute esophageal hemorrhagic ulcers were observed incidentally at the autopsy of 4 [4] elderly patients with arteriosclerotic psychosis. There had been no tube feeding, nor had operation been performed shortly before death.

CASE 1.—A woman aged 78, confused and disoriented, had been for three weeks prior to her death in the Danvers State Hospital. Autopsy revealed, besides advanced generalized and cerebral arteriosclerosis, multiple mucosal hemorrhages

4. Case 4 is classified with the cases of duodenal ulcers.

in the stomach and small and large intestine and numerous sharply demarcated, round ulcers of the lower portion of the esophagus. The necrotic areas were covered with blackish material; the edges of the ulcers had a brownish discoloration (fig. 1).

Microscopically, the esophagus in this area showed necrosis, edema, hemorrhages and accumulations of inflammatory cells, mostly polymorphonuclear leukocytes, in the mucosal and submucosal layers. Many thrombi were seen in the mucosal and submucosal veins. There was a strong reaction for hemosiderin in the superficial and deeper layers of the necrotic mucosa and submucosa, the whole necrotic area giving a dark blue reaction to the stain for iron. Weigert's fibrin stain revealed a number of gram-positive rods in the veins, which probably represented a postmortem artefact (fig. 2 *A*, *B* and *C*).

Case 2.—A white man aged 88 had been for three months in the Metropolitan State Hospital; he was confused and deteriorated all the time. Autopsy revealed

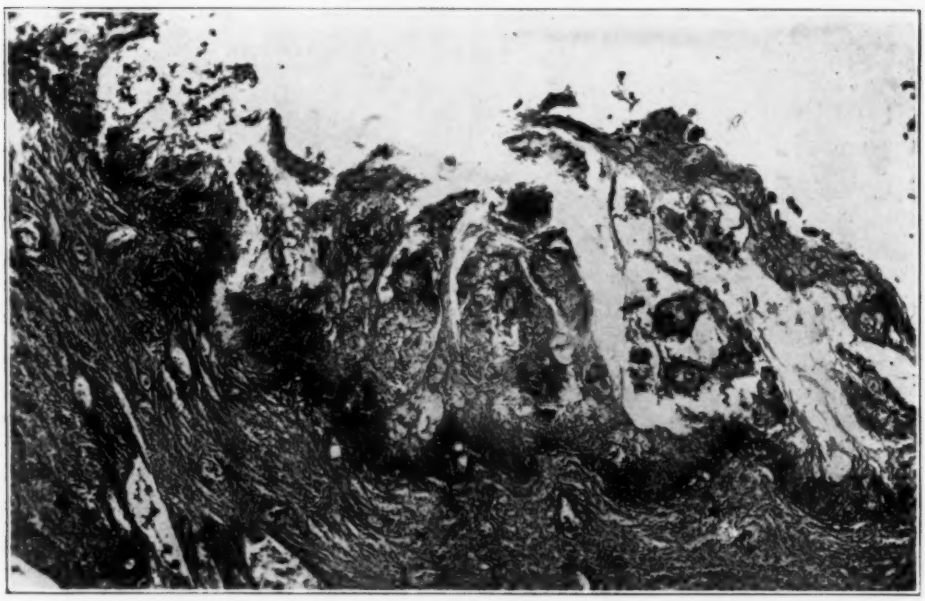


Fig. 3 (case 2).—Section of esophageal ulcer in a man aged 88 who had a psychosis, with cerebral arteriosclerosis, thrombotic softening of the right basal ganglia and confluent esophageal ulcers. The picture of necrosis, edema, cellular infiltrations and formation of hemosiderin (visible as dark bluish-stained areas) in the mucosa and submucosa is similar to that in case 1. Stain for hemosiderin; × 75.

advanced generalized and cerebral arteriosclerosis, myocardial fibrosis, terminal endocarditis, softenings of the right basal ganglia and a number of confluent ulcerations of the lower part of the esophagus, which had a brownish discoloration. One of these areas measured 3 by 2 cm. The microscopic picture of the ulcerated area of the esophagus was similar to that seen in the first case. There were also necrosis, edema, diffuse hemorrhages and accumulations of inflammatory cells in the mucosa and submucosa and some thrombi in the mucosal veins. The reaction for hemosiderin was strongly positive, staining dark blue the whole inflamed, necrotic area of the mucosa. The stain for fibrin did not reveal any organisms (fig. 3).

CASE 3.—A woman aged 93 was confused and deteriorated during her stay in the hospital. Autopsy revealed, besides general and cerebral arteriosclerosis, a large aneurysm of the abdominal aorta filled with clotted blood and multiple hemorrhagic erosions in the lower portion of the esophagus and the stomach. The microscopic picture of the esophageal ulcerations was similar to the one described in the first 2 cases. There were necrosis, edema, hemorrhages and accumulations of inflammatory cells in the mucosa and submucosa, but the reaction for hemosiderin was negative.

CASE 4.—This case, that of a man aged 73, is reported in detail later because of the accompanying duodenal ulcers. Autopsy revealed multiple thrombotic softenings in the cortex and esophageal and duodenal ulcers. The ulcers of the esophagus showed necrosis, hemorrhages, intense inflammation and a strong,

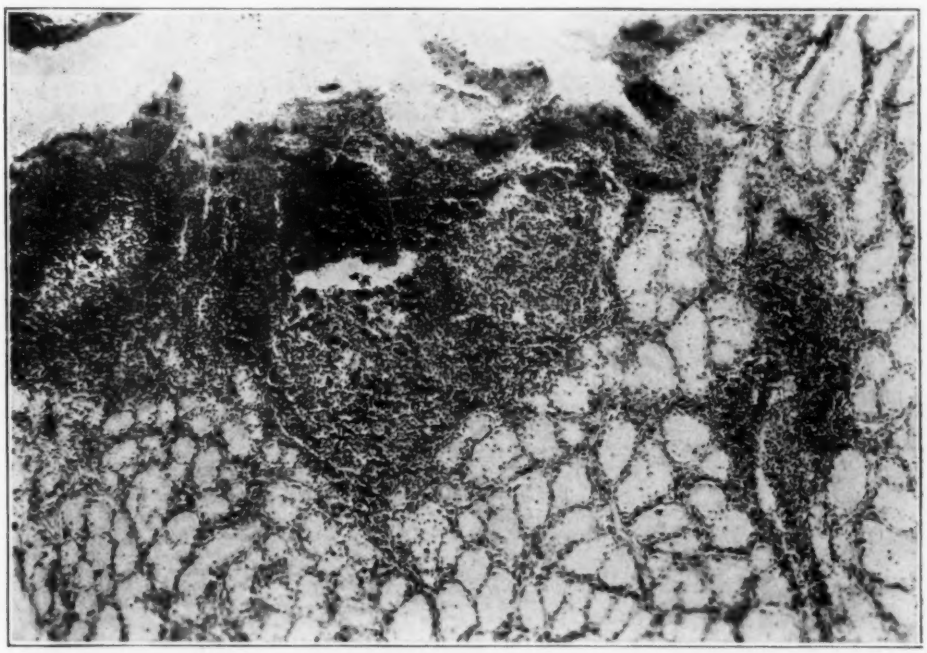


Fig. 4 (case 5).—Multiple acute hemorrhagic erosions of the stomach in a man aged 62 who had a psychosis with epilepsy. He fell forty-eight hours before death and sustained a fracture of the right middle fossa, with extradural hemorrhage over the right temporal lobe and subdural and subarachnoid hemorrhages over and contusions of the left temporal lobe. Necrosis, edema and intense cellular reaction extend from the mucosa into the submucosa. Hematoxylin and eosin stain; × 76.

diffuse bluish stain for hemosiderin in the necrotic layers, similar to that seen in the first 2 cases.

*Fundus of Stomach.*—Acute hemorrhagic gastric ulcerations in the fundus were seen in 5 elderly patients, 4 of whom had been treated for arteriosclerotic psychoses and 1 for epilepsy.

CASE 5.—A man aged 62 fell during a convulsion, hit his head and remained unconscious for forty-eight hours, when he died. Autopsy revealed fractures of the right middle and anterior fossae, extradural hemorrhage over the right

hemisphere, subdural and subarachnoidal hemorrhage over the left hemisphere and contusions of the left temporal lobe, hemorrhages into the pulmonary tissue, general and cerebral arteriosclerosis, cirrhosis of the liver and hemorrhagic erosions in the fundus of the stomach. Microscopically, the eroded area showed edema, necrosis, hemorrhages and inflammatory reaction of the mucosa and submucosa (fig. 4).

Two of the 5 patients (cases 6 and 7) were diabetic with hypertensive heart disease and died in coma.

CASE 6.—A man aged 66 with diabetes had a severe heart attack one week before his death. Autopsy revealed generalized and cerebral arteriosclerosis; coronary occlusion; old and fresh myocardial infarctions; a hypertrophic heart,

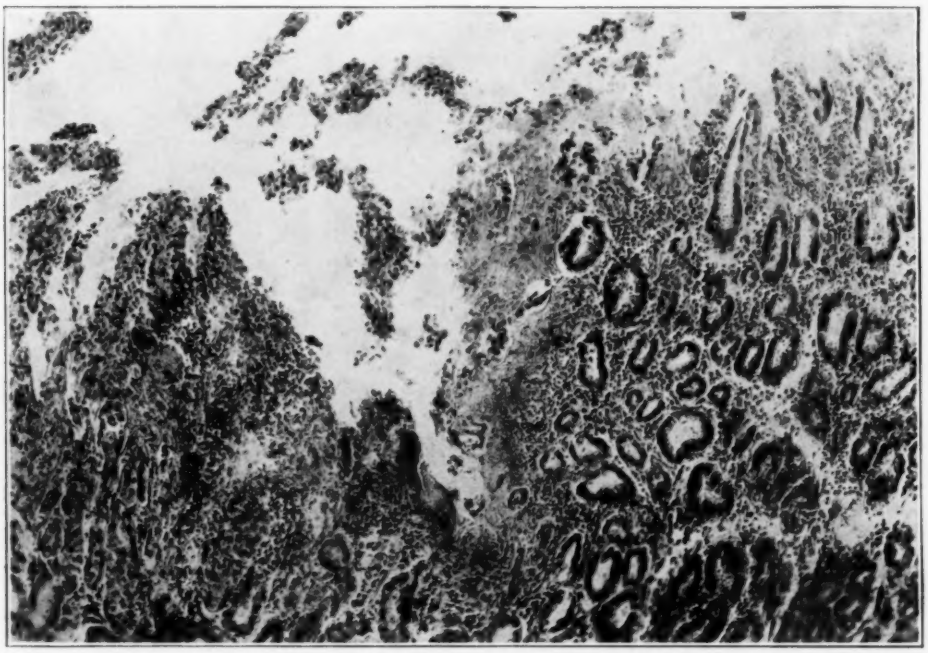


Fig. 5 (case 6).—Multiple acute gastric erosions in a man aged 66 who had a psychosis with cerebral arteriosclerosis, thrombotic softening of the right basal ganglia, coronary occlusion and myocardial infarction of one week's duration. The necrosis, edema and cellular infiltration of the mucosa are more superficial than in case 5 (fig. 4). Hematoxylin and eosin stain; × 77.

weighing 750 Gm.; softenings of the right basal ganglia, and a number of hemorrhagic ulcerations in the fundus of the stomach. The microscopic picture was similar to the one seen in the first case. The reaction for iron was negative (fig. 5).

CASE 7.—A man aged 77 with diabetes vomited blackish fluid before his death and died in coma. Autopsy revealed generalized and cerebral arteriosclerosis, hypertrophic heart, softenings of the right basal ganglia and numerous hemorrhagic ulcerations in the fundus of the stomach. The microscopic picture was not different from the one observed in the other cases, with necrosis, edema, hemorrhages and accumulations of inflammatory cells in the mucosa and submucosa.

CASE 8.—A woman aged 84 sustained a fracture of the hip two months prior to her death. She was confused and deteriorated and died in coma. Autopsy revealed advanced generalized and cerebral arteriosclerosis, softenings of the right occipital lobe and a few hemorrhagic ulcerations in the stomach below the cardia. The microscopic picture of the ulcerated area was similar to the one seen in the other cases.

The fifth case should be considered separately because local pathologic changes could explain the occurrence of the gastric ulcerations.

CASE 9.—A man aged 78 collapsed one afternoon and died within twenty-four hours after the onset of the symptoms, which consisted in repeated vomiting and general weakness. Autopsy revealed, besides generalized and cerebral arteriosclerosis, acute dilatation of the stomach and the upper portion of the jejunum and an obstruction of the jejunum by old fibrous adhesions. There were multiple small ulcerations in the fundus of the stomach below the cardia.

Microscopically, there were necrosis, edema, diffuse hemorrhages and accumulations of inflammatory cells in the mucosa and submucosa. A few thrombi were seen in the mucosal veins. The reaction for hemosiderin was negative. The mucosa at one of the ulcers was covered by metaplastic squamous cell epithelium. Otherwise, the picture was not different from that in the other 4 cases.

In 4 out of 6 cases studied at the office of the Chief Medical Examiner of New York City, the acute hemorrhagic ulceration of the stomach followed skull fractures with subdural and subarachnoid hemorrhages and lacerations of the brain. In 1 case the ulcers were associated with a spontaneous cerebral hemorrhage, and in another case, with a subarachnoid hemorrhage. The ages of the 6 patients varied from 40 to 74 years; all the patients had been unconscious for more than twenty-four hours before death. Thus, acute gastric ulcerations were associated with the following cerebral lesions: cerebral lacerations, with traumatic subdural and subarachnoid hemorrhages, 5 cases; spontaneous cerebral hemorrhage, 1 case; subarachnoid hemorrhage, 1 case; cerebral arteriosclerosis and thrombosis, 3 cases; cerebral arteriosclerosis and acute intestinal obstruction, 1 case.

*Duodenal Ulceration.*—Twelve cases of acute hemorrhagic duodenal ulcerations were seen in association with the following cerebral lesions: traumatic cerebral lacerations with subdural and subarachnoid hemorrhages, 4 cases; cerebral thrombosis, 4 cases; acute purulent meningitis, 1 case; advanced cerebral arteriosclerosis, 2 cases; meningioma, 1 case. All the patients had been in a state of coma or unconsciousness for several hours or longer before death. Tarry stools were present in all cases. Ages of patients in state hospitals for mental diseases ranged from 16 to 93 years; the ages in the Medical Examiner's series, from 42 to 77 years. The duodenal ulcers were multiple, superficial, circular or linear and were situated in the first third of the duodenum. They were covered with a blackish material. No ulcer had perforated. The microscopic picture was similar in all cases. There were necrosis, edema, hemor-

rhages and accumulations of inflammatory cells through the mucosa and submucosa and thrombi in the mucosal veins. The blood in the vessels and the necrotic mucosa was often brownish. The reaction for hemosiderin was negative in all cases.

CASE 10.—The youngest patient in the series, a youth aged 16, died on the sixth day in the hospital, of pneumococcic meningitis. Autopsy revealed purulent exudate covering the whole surface and base of the brain, which was swollen (weight, 1,530 Gm.). There were also hemorrhagic, pneumonic areas in both lungs, an acute tumor of the spleen and multiple circular hemorrhagic ulcerations in the upper portion of the duodenum. The microscopic picture of the ulcer was that already described (fig. 6 *A* and *B*).

The other 5 patients in the present series had an arteriosclerotic psychosis, and 3 of them had been in coma because of cerebral thrombosis for several days before death.

CASE 11.—A woman aged 66 had been unconscious and paralyzed on the left side for five days. Autopsy revealed generalized and cerebral arteriosclerosis, a large thrombus in the abdominal aorta, thrombotic softening of the whole right hemisphere and multiple hemorrhagic ulcerations in the upper portion of the duodenum.

CASE 12.—A man aged 88 was admitted in a semicomatose condition to the hospital and died three days later. Autopsy revealed advanced general and cerebral arteriosclerosis with softenings of the right basal ganglia, which were probably three weeks old. There were multiple linear and circular hemorrhagic ulcerations in the upper part of the duodenum (fig. 7 *A* and *B*), with a microscopic picture in the region of ulceration similar to that in the other cases.

CASE 13.—A man aged 93 was for three months in the hospital, confused and disoriented all the time. Autopsy revealed generalized and cerebral arteriosclerosis, softening of the right basal ganglia, caseous tuberculosis of the lungs, multiple linear hemorrhagic ulcers in the upper portion of the duodenum, which grossly and histologically gave the same picture as that in all the other cases, namely, necrosis, edema, hemorrhages and intense inflammation of the mucosa and submucosa associated with thrombi in the mucosal veins.

CASE 14.—A white woman aged 66 had been confused and stuporous during the last days before her death. Autopsy revealed general and cerebral arteriosclerosis, a carcinoma of the uterus with metastases to the regional lymph nodes and numerous linear hemorrhagic ulcers in the upper portion of the duodenum.

CASE 4.—A man aged 73 was deteriorated and confused and in coma twenty-four hours prior to death. Autopsy revealed generalized and cerebral arteriosclerosis, multiple thrombotic softenings in various parts of the brain, adhesive pericarditis, terminal endocarditis and a few hemorrhagic circular ulcers in the upper portion of the duodenum and blackish discolored, confluent ulcers of the lower portion of the esophagus, the microscopic picture of which has been already described.

Microscopically, the ulcerated areas in the duodenum in the last 2 cases showed the same picture as was observed in the other cases.

In 4 out of 6 cases observed at the Office of the Chief Medical Examiner of New York City, the acute hemorrhagic duodenal ulcerations

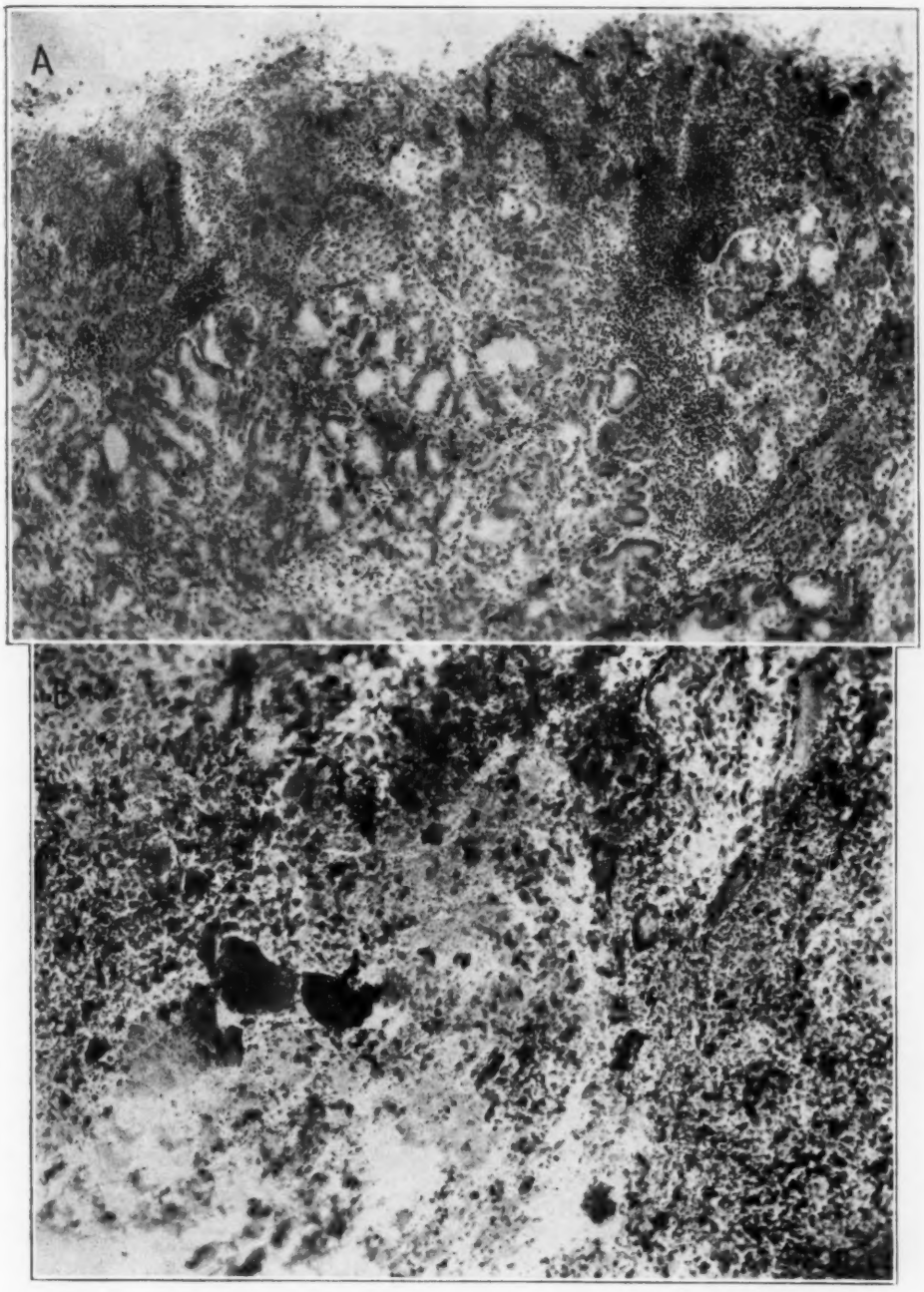



Fig. 6 (case 10).—*A*, section from the region of the duodenal ulcer in a youth aged 16, who had purulent pneumococcic meningitis and multiple circular hemorrhagic duodenal ulcers. Necrosis, edema, cellular infiltrations and thrombi in the mucosal and submucosal layers are visible. Hematoxylin and eosin stain; × 77.

*B*, higher magnification (× 165) of a portion of the same section as that in *A*, showing necrosis, edema, cellular infiltrations and thrombi in the veins of the mucosa and submucosa.

followed skull fractures with subdural and subarachnoid hemorrhages and cerebral lacerations. In 1 case they were associated with a thrombotic softening of the right hemisphere, and in another case with edema of the brain caused by meningioma. All 6 patients had been in coma from fourteen hours to four days prior to death. Thus, in the 26 cases

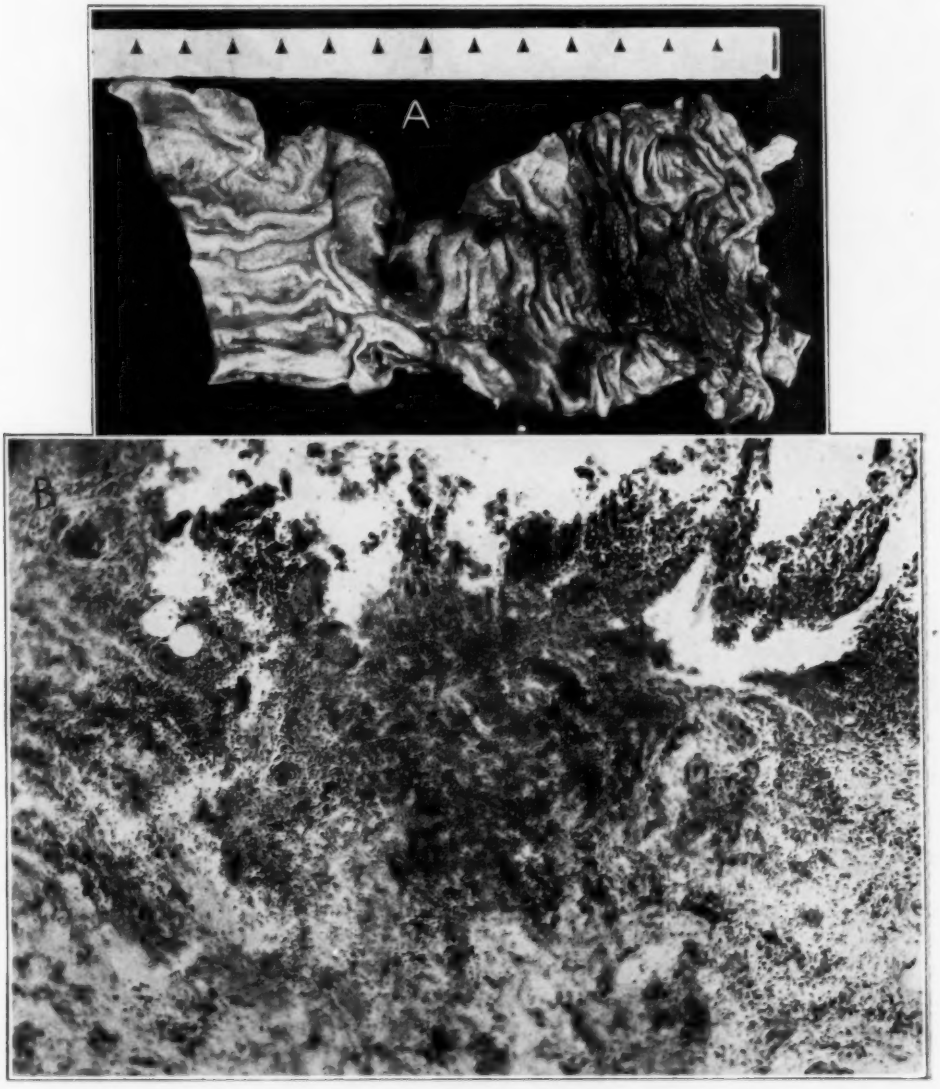



Fig. 7 (case 11).—*A*, duodenum with multiple terminal acute hemorrhagic ulcers, circular and linear, in a man aged 88, who had a psychosis with cerebral arteriosclerosis. Autopsy revealed thrombotic softening of the right basal ganglia of three weeks' duration.

*B*, region of the ulcer, showing intensive cellular infiltration, diffuse hemorrhages, necrosis and edema of the mucosa and submucosa. Hematoxylin and eosin stain; × 76.

acute hemorrhagic ulcerations of the upper gastrointestinal tract were associated with the following cerebral lesions: cerebral arteriosclerosis, 4 cases; cerebral thrombosis, 9 cases; traumatic cerebral lacerations, with subdural and subarachnoid hemorrhages, 9 cases; cerebral spontaneous hemorrhage, 1 case; subarachnoid hemorrhage, 1 case; meningioma, 1 case; purulent meningitis, 1 case.

Dark brownish fluid and tarry stools were present in all 26 cases, but the diagnosis of ulceration had not been made during life. In the majority of the cases there were sclerosis, thickening and narrowing of the lumen of the arterioles of the esophagus, stomach or duodenum. The reaction for iron was negative in all but the 3 cases of esophageal ulcer, in which Gömöri's stain for hemosiderin gave the unusual picture of diffuse bluish staining of the necrotic area, especially of the vessel walls and the fibrous connective tissue of the submucosa.

GROUP 5.—In 10 out of 196 cases (or 5.1 per cent) autopsy showed advanced gastromalacia, although the wall of the stomach had not ruptured. The following lesions of the brain were observed: cerebral arteriosclerosis and thrombosis, 7 cases; multiple sclerosis, 1 case; Alzheimer disease, 1 case; edema of the brain in a catatonic state, 1 case. The stomach contained dark brownish fluid in all cases and microscopically showed necrosis, brownish discoloration, edema and some accumulations of inflammatory cells in the mucosa and submucosa. Sixty cases of advanced esophagomalacia and gastromalacia were collected from 1,200 autopsies observed at the Chief Medical Examiner's Office of New York City during a two year period. In 30 of these cases the esophagus or stomach had ruptured and brownish fluid was noted in the abdominal or the pleural cavity, which had digested the spleen, the diaphragm, the pleura or the lungs. In these 30 cases nontraumatic ruptures of the esophagus or stomach were associated with the following intracranial lesions: skull fractures, subdural and subarachnoid hemorrhages and lacerations of the brain, 15 cases; spontaneous subarachnoid hemorrhages, 3 cases; acute purulent meningitis, 3 cases; cerebral thrombosis, 1 case; meningioma, 1 case; cerebral abscess, 1 case; acute encephalitis, 1 case; fracture of the cervical portion of the spine with crushing of the cord, 1 case; barbiturate poisoning, 2 cases; septicemia after burns, 1 case, and emphysema with purulent bronchitis, 1 case, that of a man aged 76.

Thus, in 25 out of 30 cases traumatic or spontaneous severe intracranial lesions were observed. The case of crushing of the cord and the 2 cases of fatal barbiturate poisoning should be included with the cases of intracranial lesions. Therefore, in only 2 cases of rupture of the esophagus or stomach was no gross intracranial lesion apparent. The ages of the 30 patients at death varied from 20 to 76 years.

COMMENT

It has long been known that acute hemorrhagic erosions and softenings of the upper gastrointestinal tract are occasionally seen in connection with cerebral lesions.[5] Eleven such cases in man were reported by Cushing [1] and 8 similar cases were recently described by Masten and Bunts.[3] Hemorrhagic ulcerations of the stomach and duodenum have been observed in animals after experimentally produced mechanical or chemical stimulation of autonomic centers or fibers [2] and after head injuries.[6] Such stimulation causes spasm of gastrointestinal vessels, followed by ischemic necrosis of the mucosa, vasodilatation, edema and diapedetic hemorrhages. Small mucosal hemorrhages of the gastrointestinal tract were frequently seen in this autopsy material under varying conditions. They have no special significance and should be considered a terminal or agonal phenomenon. However, they have more importance if they lead to gross bleeding into the lumen of the stomach or intestine. In 24 of 196 cases with autopsy this gross bleeding was observed, and in 9 cases it was associated with intracranial lesions of various types. Hemorrhagic ulcerations were observed when the vascular disturbances were of a severer nature and had lasted for a longer period. The gross picture was that of multiple, superficial, circular or linear erosions covered with blackish material.

These erosions were situated in various areas of the lower portion of the esophagus, the fundus of the stomach or the upper part of the duodenum. No perforated ulcers were seen. In number, appearance, size and site of occurrence, the erosions differed from the picture usually given by peptic ulcers of the stomach and duodenum. Microscopically, all these ulcerations were characterized by necrosis, edema, hemorrhages, formation of venous thrombi and an intense cellular reaction (inflammation), extending from the mucosa through the submucosa. In the majority of cases the ulcerations had been formed apparently shortly before death, for the reaction for hemosiderin was negative in all but 3 cases of esophageal ulcer. In these 3 instances the stain for hemosiderin gave a diffuse bluish discoloration of the whole necrotic area of the mucosa and submucosa; vessel walls and connective tissue fibers became intensely blue with the Perles test. This picture was quite different from the one usually seen in hemorrhagic areas of other organs, and it has not been described in cases of esophageal ulcer reported by

5. Beneke, R.: Ueber die hämorrhagischen Erosionen des Magens (Stigmata ventriculi), Verhandl. d. deutsch. path. Gesellsch. **12**:284, 1908. Roessle, P. R.: Das runde Geschwür des Magens und Zwölffingerdarmes als "Zweite Krankheit," Mitt. a. d. Grenzgeb. d. Med. u. Chir. **25**:766, 1912. Ewalt, J. R.: Psychosomatic Problems, J. A. M. A. **126**:150 (Sept. 16) 1944. Cushing.[1]

6. Tedeschi, C.: Gastric Mucosal Lesions in Rats Submitted to Head Trauma, Proc. Soc. Exper. Biol. & Med. **57**:268 (Nov.) 1944. Footnote 2.

other authors.[7] As a rule, hemosiderin is always observed within histiocytes. The diffuse bluish coloring of the tissues with the hemosiderin stain cannot be considered an artefact, because it was seen with an intense inflammatory reaction only in these 3 cases of esophageal ulcer, which were fixed, cut and stained at different times. No reaction to prussian blue was obtained in any of the other cases.

The patients in whom ulcerations or softenings of the gastrointestinal tract were observed had been unconscious or in coma for hours or days before death. The ages of the patients ranged from 16 to 93 years, but patients over 60 years of age with arteriosclerotic changes in the gastrointestinal vessels provided most of the material. The importance of the arteriosclerotic factor in the occurrence of bleeding peptic ulcers was recently stressed by Wangensteen.[8] Ulcerations of the esophagus, stomach and duodenum have been reported under a variety of primary conditions, after operations and in connection with shock.[7] However, the present material proves that under various traumatic or spontaneous pathologic intracranial conditions hemorrhagic ulcerations and softenings of the gastrointestinal tract occur. They were seen after traumatic lacerations of the brain with subdural and subarachnoid hemorrhages, spontaneous subarachnoidal hemorrhages, spontaneous cerebral hemorrhages, cerebral thrombosis and arteriosclerosis, cerebral tumor, purulent meningitis, cerebral abscess, acute encephalitis and barbiturate poisoning. Gross lesions of the brain were absent in only 2 out of 30 cases of perforation of esophagus or stomach. There is no explaining why gastrointestinal ulcerations and softenings were not observed more often in connection with these intracranial lesions when the same

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7. Pringle, J.; Stewart, L., and Teacher, J. H.: Digestion of the Esophagus as a Cause of Postoperative and Other Forms of Hematemesis, J. Path. & Bact. **24**:396 (Oct.) 1921. Bartels, E. C.: Acute Ulcerative Esophagitis: Pathologic and Clinical Study of Eighty-Two Cases Observed at Necropsy, Arch. Path. **20**:369 (Sept.) 1935. Butt, H., and Vinson, P.: Esophagitis: Anatomy and Physiology and Review of Literature, Arch. Otolaryng. **23**:391 (April) 1936. Bloch, L.: Acute Ulcerative Esophagitis, Am. J. Digest. Dis. **7**:407 (Oct.) 1940. Penner, A., and Bernheim, A.: Acute Postoperative Esophageal Gastric and Duodenal Ulcerations: Further Study of Pathologic Changes in Shock, Arch. Path. **28**:129 (Aug.) 1939; Acute Postoperative Enterocolitis: A Study on Pathologic Nature of Shock, ibid. **27**:966 (June) 1939. Dick, R. C., and Hurst, A.: Chronic Peptic Ulcer of the Esophagus and Its Association with Congenitally Short Esophagus and Diaphragmatic Hernia, Quart. J. Med. **11**:105 (April) 1942. Chamberlin, D. T.: Peptic Ulcer of the Esophagus, Am. J. Digest. Dis. **5**:725 (Jan.) 1939. Feldman, M.: Peptic Ulcer of the Lower Esophagus Associated with Esophageal Hiatus Hernia: Report of Two Cases, Am. J. M. Sc. **198**:165 (Aug.) 1939.

8. Wangensteen, O. H.: The Ulcer Problem: Etiology with Special Reference to Inter-Relationship Between Vascular and Acid-Peptic Digestive Factors; Characterization of Satisfactory Operation Which Will Protect Against Recurrent Ulcer (Listerian Oration), Canad. M. A. J. **53**:309 (Oct.) 1945.

pathologic conditions involving the brain or the meninges were seen in cases with and without ulcerations or softening of the gastrointestinal tract. It seems likely that autonomic centers and fibers can be stimulated under varying conditions—by direct pressure from hemorrhages or exudates or by disturbances of blood supply, thrombosis, anoxemia, edema or inflammation. Hemorrhagic ulcerations or softenings of the esophagus, stomach or duodenum followed such stimulation in several instances. The reason that none of these ulcerations or softenings had been diagnosed during life could be seen in the disturbed or comatose condition of the patients.

During the preparation of this paper, hemorrhagic, ulcerative esophagitis was observed in a patient aged 64 with Alzheimer disease; hemorrhagic acute terminal duodenal ulcers were seen in 3 patients with cerebral arteriosclerosis and multiple thrombotic softenings, and advanced gastromalacia was seen in several patients, in 1 of whom perforation of the stomach and digestion of the spleen, diaphragm and left lung, associated with spontaneous cerebral hemorrhage of two days' duration, were observed.

SUMMARY

In a large autopsy material, the coincidence of intracranial lesions with and their relationship to acute hemorrhagic ulcerations and softenings of the gastrointestinal tract were studied. Mucosal hemorrhages of the stomach, duodenum and other parts of the intestine were frequently encountered in routine autopsies; they were a terminal phenomenon occurring under a variety of conditions. More important were advanced stages of vascular disturbances involving the esophagus, stomach and duodenum, such as gross bleeding from mucosal hemorrhages, hemorrhagic ulcerations or softenings with perforations. These lesions were observed in association with various injuries and diseases of the meninges and brain. In cases of ulcer formation, microscopically, an intense inflammatory reaction, hemorrhages and venous thrombi were noted in and near the necrotic area. In cases of softening, the necrosis of the wall extended through all layers, and the inflammatory reaction was insignificant. It seems likely that autonomic centers had been stimulated in a variety of pathologic intracranial conditions and that the irritation had produced mucosal hemorrhages or ulcerations or softenings of the gastrointestinal tract or a combination of such lesions. In this paper, 26 cases of acute hemorrhagic ulcerations and 30 cases of softenings and perforations of the esophagus, stomach and duodenum are reported. In all but 2 cases the gastrointestinal lesions were associated with intracranial lesions of various natures. Hemosiderin was observed in 3 cases of esophageal ulcer, staining diffusely the necrotic area. In all other cases the reaction for hemosiderin was negative.

Metropolitan State Hospital.

# ABREACTION IN THE MILITARY SETTING

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IN THEIR epoch-making work on hysteria, Freud and Breuer first used the term "abreaction" to describe the intense reproduction, under hypnosis, of the original emotion accompanying the recollection of traumatic experience.[1] Recently, with the increased use of intravenously injected barbiturates in the treatment of war neuroses, the importance of abreaction as a therapeutic measure has been stressed. It is basic in narcosynthesis,[2] or narcoanalysis,[3] and in hypnoanalysis.[4] The purpose of this paper is not to review the literature dealing with the subject but, rather, to present a brief outline of our experiences with, and our conclusions about, the use of abreaction in the treatment of combat-precipitated neuroses in the only general hospital in the European Theater of Operations in which the total case load was continuously neuropsychiatric.

Abreactive therapy seemed especially valuable as an initial step in the treatment of acute battle reactions with pronounced amnesias, severe anxiety states, hallucinatory experiences, regressive phenomena, apparently psychotic episodes or severe conversion symptoms. In most cases, however, the abreacted material had to be utilized immediately. We have occasionally seen improvement when the patient was allowed to fall asleep at the end of a session, but in our experience such a procedure usually has no more curative value than a half-forgotten nightmare (cases 3 and 5). We have found it a *sine qua non* of abreaction with the barbiturates to keep the patient awake and to bring about immediate recall, in the waking state, of the material uncovered under narcosis. When intravenously injected barbiturates are used, the physician who is too busy to remain until the effects of the drug wear off can assign a corpsman or a nurse, or even another patient, to stay with the soldier

1. Hendrick, I.: Facts and Theories of Psychoanalysis, ed. 2, New York, Alfred A. Knopf, 1944.

2. Grinker, R. R., and Spiegel, J. P.: War Neurosis in North Africa—The Tunisian Campaign, New York, Josiah Macy Jr. Foundation, 1943.

3. Minski, L.: War Neuroses, Am. J. Psychiat. **101**:600, 1945.

4. Hadfield, J. A.: Treatment by Suggestion and Hypno-Analysis, in Miller, E.: The Neuroses in War, London, Macmillan and Company, Ltd., 1940, chap. 7.

who has abreacted, to walk and to talk with him and to keep him awake. Kubie [5] stated:

> . . . whatever the method used, whether it is hypnosis alone, hypnosis under narcosis or hypnagogic reveries with or without narcosis, the recovered material must be fully fused with its appropriate emotional content and with normal waking consciousness.

To us, the most important aspect of abreactive therapy, so called, consists in the ultimate aeration of conflict material on the conscious level. This is of prime importance when conversion symptoms are removed and underlying anxiety, with or without depression, comes to the fore. It is even more important when symptomatic recovery, partial or complete, is achieved after an abreaction or a series of abreactions. Valuable as emotional catharsis has proved itself to be, it must, nevertheless, be considered merely one stage in a therapy which has as its goal the reintegration of the total personality of the patient under treatment.[6]

Abreaction may be spontaneous, suggested under hypnosis or induced with drugs. Some patients abreact spontaneously. Months after leaving the line, they repeatedly hallucinate themselves back into menacing, terror-laden combat situations for which otherwise they seem completely amnestic. Sudden, unexpected noises, like the slamming of a door, can constitute the stimulus (case 1). Perhaps a mere drink or two of an alcoholic beverage may precipitate the abreaction. So may superficially innocuous discussions about combat (cases 2 and 3). Raines and Kolb [7] stated that abreaction in their cases was obtained, on a conscious level for the most part, by individual psychotherapeutic sessions during which the patient was brought to relive his battle experience.

In our experience, however, conscious abreaction of this type cannot be affected quite so universally as these authors seem to believe. With most of the combat-precipitated psychiatric casualties seen at this installation, abreaction must be induced. Various pharmacologic agents have been recommended. In forward areas, the British used ether.[3] Psychiatrists in the Red Army apparently also made use of this drug.[8] Nitrous

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5. Kubie, L. S.: Manual of Emergency Treatment for Acute War Neuroses, War Med. **4**:582 (Dec.) 1943.

6. (*a*) Kubie.[5] (*b*) Grinker, R. R., and Spiegel, J. P.: Brief Psychotherapy in War Neuroses, Psychosom. Med. **6**:123, 1944. (*c*) Grinker, R. R.: Treatment of War Neuroses, J. A. M. A. **126**:142 (Sept. 16) 1944. (*d*) Grinker, R. R., and Spiegel, J. P.: War Neuroses in Flying Personnel Overseas and After Return to the U. S. A., Am. J. Psychiat. **101**:619, 1945.

7. Raines, G. N., and Kolb, L. C.: Treatment of Combat Induced Emotional Disorders in a General Hospital Within the Continental Limits, Am. J. Psychiat. **101**:331, 1944.

8. Zilboorg, G.: Some Aspects of Psychiatry in the U. S. S. R., Am. Rev. Soviet Med. **1**:562, 1944.

oxide has been tried.[9] Scopolamine hydrobromide has been used in combination with morphine sulfate.[5] Alcohol has at times been called the drug of choice,[10] but with acute combat casualties its use is obviously contraindicated because of the danger of cerebral involvement. The barbiturates are now being administered, orally and intravenously, on a wide scale.[11]

Nevertheless, suggestion hypnosis constitutes the simplest abreactive agent. We have seen few patients who could not be hypnotized at first trial within, at the most, a five minute period, provided that symptoms seemed of the type for which abreactive therapy was indicated as part of the treatment program. Ready suggestibility seems almost characteristic of such patients, whether they show psychotic-like pictures or not, and this is especially true of acute battle casualties with pronounced regressions. Technics are simple and can readily be learned, even without formal instruction.[12] On the other hand, it appears at times practically impossible to hypnotize soldiers hospitalized for medicolegal reasons by order of a court martial, and it seems almost as impossible to hypnotize patients completely out of contact because of severe and all-enveloping depressions, equally severe regressions or confusional states with extreme disorientation. For such patients, intravenous injection of a barbiturate is indicated, at least for the initial abreaction. With most patients, suggestion hypnosis can be utilized during subsequent sessions (case 4).

Abreaction under suggestion hypnosis, in our experience, cannot be distinguished clinically from the abreaction induced with pentothal or amytal.[13] Lambert and Rees [14] utilized both verbal hypnosis and narcosis induced by intravenous injection of barbiturates in 247 cases of hysteria and found no significant difference. Erickson [10] urged more extensive utilization of hypnosis as a therapeutic procedure and stressed its

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9. Rogerson, C. H.: Narcoanalysis with Nitrous Oxide, Brit. M. J. **1**:811, 1944.

10. Erickson, M. H.: Hypnotic Techniques for the Therapy of Acute Psychiatric Disturbances in War, Am. J. Psychiat. **101**:668, 1945.

11. Grinker and Spiegel.[2] Minski.[3] Kubie.[5] Grinker and Spiegel.[6b, d]

12. Brenman, M., and Gill, M. M.: Hypnotherapy, New York, Macy Foundation Review Series, 1944, vol. 2, no. 3, chap. 3.

13. Two of our patients had abreacted first under amytal narcosis, then under suggestion hypnosis and, finally, under amytal narcosis again. On each occasion, the abreaction was apparently of the same intensity. Near the end of each abreaction, the patient was given the same posthypnotic (or, rather, postabreactive) suggestion, to be carried out twenty-four hours later. The suggestion was ignored after amytal narcosis, but not after hypnosis. For obvious reasons, however, no conclusions can be drawn from so isolated an experiment.

14. Lambert, C., and Rees, W. L.: Intravenous Barbiturates in the Treatment of Hysteria, Brit. M. J. **2**:70, 1944.

advantage over the use of narcotic drugs. It is interesting to note that psychiatrists now seem to be returning to the hypnotic therapy first used by Breuer and Freud.

With the United States Army in the European Theatre of Operations, intravenously injected barbiturates appear to have been the most commonly utilized abreactive agents. To a large extent, this seems to have been due to the significant work of Grinker and Spiegel.[15] With cases of the type encountered in our wards, barbiturates were not often necessary. In soldiers who abreact on the mere injection of the drug. conflict material is probably so close to the surface that aeration can usually proceed on the conscious level. Acutely ill patients, especially those with pronounced amnesia, confusion, hallucinations and other superficially psychotic symptoms, can usually be hypnotized in less time than it takes to sterilize the skin, inject the drug and induce the abreaction. We believe, therefore, that intravenous injection of barbiturates is indicated under the following conditions: (*a*) when the patient is completely out of contact or when he is uncooperative for medicolegal or other reasons; (*b*) when suggestion hypnosis has already been unsuccessfully attempted, or (*c*) when the therapeutist lacks training in hypnotic technics or confidence in his ability to use them.

Grinker and Spiegel preferred pentothal as the abreactive agent because its effects wear off quickly, permitting continuance of psychotherapy immediately after the discussion of battle experiences.[2] So far as we can determine, it makes little difference whether amytal or pentothal is injected. Amytal occasionally works when pentothal is without effect, and vice versa. Occasionally, neither hypnosis nor intravenous injection of barbiturates is sufficient. In such cases, intravenous administration of drugs with superadded suggestion hypnosis may be efficacious. This should always be tried. However, failures occur. In 1 of our cases repeated injections of amytal and pentothal, in conjunction with as often repeated concurrent attempts at hypnosis, were completely unsuccessful. Again, occasional patients abreact but, despite strong suggestion, remain amnestic for both abreaction and events abreacted, and these patients often fail to show symptomatic improvement (case 5). In failures of this type, electric shock seems to effect a partial remission, as a result of which the patient becomes more accessible to other forms of psychotherapy. We believe, therefore, that electric convulsive therapy is of value for patients with psychotic or psychotic-like pictures which have not responded to abreactive therapy. Electric shock seems to be of aid, however, primarily in helping the patient repress his traumatic experiences, rather than aerate them. Abreaction successfully induced in 2 such patients after partial remis-

15. Grinker and Spiegel (footnotes 2 and 6 *b* and *d*) Grinker.[6e]

sions had been effected seemed to reprecipitate the original symptoms (case 6); and, in our opinion, abreactive therapy either is contraindicated after electric shock or should be used with extreme caution, although this opinion may have little validity because of the small number of patients so studied.

There seem to be four other contraindications to the use of abreactive therapy in the military setting. Concisely, these may be stated as follows: 1. A number of combat-precipitated psychiatric casualties show anxiety and depression without bizarre coloration. Treatment of symptoms on a conscious level is much less dramatic, but symptomatic improvement is usually just as rapid and just as pronounced. If a sense of ignominy and frustration about enforced withdrawal from combat is superadded, repressive technics may at times be indicated.[16] 2. Some patients show startle reactions so pronounced that at times they seem to be climbing up walls, hanging on rafters or cowering under chairs and bedding. Such patients are to all intents and purposes abreacting spontaneously. They require heavy sedation, at least for a few days, after which they become much more approachable. By this time, abreaction may no longer be indicated, although for some patients it seems invaluable. 3. We do not believe it necessary to clear up every amnesia. Amnesia may represent an attempt to repress and forget painful emotional experience. As a result, we feel justified in using abreactive technics in the treatment of such amnesia only when the patient himself consciously desires to remember, is disturbed by his failure to remember or shows by the overt symptoms of anxiety, depression and the like, that the process of repression is unsuccessful. 4. Finally, in our experience, abreactive therapy of the type possible in the military setting is of little value in the treatment of chronic neuroses or of vague hypochondriacal syndromes.

Our discussion up to this point has been concerned primarily with indications and contraindications to the use of abreaction as the first step in the treatment of severe combat-precipitated psychiatric casualties. Military physicians have at times utilized this particular therapeutic procedure, without deeper or adjuvant therapy, for the "cure" of hysterical paralyses and other conversion symptoms. Whether such therapy, so called, is of much importance in the absence of free-floating anxiety is a problem which warrants further investigation. We have seen too many failures, in men transferred to this installation from other hospitals or sent back to duty and almost immediately rehospitalized, to be impressed. A complete reorientation of the total personality seems in

16. Needles, W.: A Statistical Study of One Hundred Neuropsychiatric Casualties from the Normandy Campaign, Am. J. Psychiat. **102**:214, 1945.

order, not merely the removal of a symptom serving to mask deep underlying insecurity, anxiety and even potentially suicidal depression.

All authors [17] have stressed the importance of concomitant psychotherapy.[18] Grinker and Spiegel [6b] stated:

> The idea that narcosis therapy of any form of abreaction is all that is necessary for the treatment of the acute war neuroses is erroneous, as proven by the fact that if nothing else is done for the patient he relapses. . . . Psychotherapy must be instituted as soon as possible.

Heath and Sherman [19] stated that they found narcosynthesis disappointing and that "it often causes the patient to go beyond the war experience, stirring up old neurotic conflicts which may merge with the war reaction, thereby adding to the danger of chronicity." This seems to us to ignore the fact that war neuroses do not arise *de novo,* but bear a fundamental relation to the previous personality and to old conflicts. This was clearly recognized and expressed by Grinker and Spiegel.[6d]

> The associations [under pentothal] clearly bring out the dynamic relationship between the new neurotic reaction and the old character neurosis or psychoneurotic pattern which are the real perpetrators of the vicious cycle of anxiety. We are unsatisfied now until the patient becomes aware with emotional insight of the relationship between his reaction to inter-personal problems in the combat squadron and his old patterns or until he gains insight into these ancient dynamic forces.

Parenthetically, we might add that we have failed to see the benefit from ergotamine claimed by Heath and Sherman.[19]

Abreaction is not only a therapeutic weapon but a diagnostic one as well. Whether or not it can be used indiscriminately to detect the malingerer, as some authors have apparently claimed, raises a problem which we should like to discuss in detail in another paper, especially in view of the fact that at times malingering itself may constitute a symptom. Abreaction, nevertheless, has a definite place in the investigation of certain types of medicolegal cases. Ludwig [20] expressed the belief that with intravenous injection of barbiturates the malingerer resists narcosis and is unproductive and negativistic, in contrast to the

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17. Morris, D. P.: Intravenous Barbiturates: An Aid in the Diagnosis and Treatment of Conversion Hysteria and Malingering, Mil. Surgeon **96**:509, 1945. Grinker and Spiegel.[2] Minski.[3] Hadfield.[4] Grinker and Spiegel.[6b] Grinker.[6c] Raines and Kolb.[7]

18. Psychotherapy often involved definite reassurance that the patient would not be returned to combat duty,[6b] and this was particularly true for the conversion states.

19. Heath, R. G., and Sherman, S. H.: The Use of Drugs in the Treatment of Traumatic War Neuroses, Am. J. Psychiat. **101**:355, 1944.

20. Ludwig, A. C.: Clinical Features and Diagnosis of Malingering in Military Personnel: Use of Barbiturate Narcosis as an Aid in Detection, War Med. **5**: 378 (June) 1944.

neurotic patient, who "opens up" and becomes productive. Morris [17] agreed with Ludwig and cited several cases. These are unconvincing. On the evidence presented, we should certainly never call his case 3 one of malingering, and we feel doubtful about his case 5. Hartman's [21] experience seems of value in connection with this problem of malingering. He dealt with all prisoners sent to this hospital, several of whom claimed amnesia for their alleged offense. When the patient was assured that the medical officer wished to help him with his legal difficulties and that of course he, the patient, wished to recover his memory, it was possible in every case to clear up the amnesia, provided the examiner was persistent enough and the drug was pushed to a deep enough level. At first, this frequently necessitated the use of large amounts of amytal or pentothal. Later, it was found that with a combination of verbal hypnosis and drug narcosis the same results could be obtained with much smaller amounts of the drug. It was of interest that in patients suspected of malingering the first productions were bizarre and disconnected. Then, often in a sudden burst, a clear, connected story was obtained. This work contradicts Ludwig's claim that malingerers are always nonproductive, and the results are probably due to differences in the technics used.

Abreaction can also often be used as a definite aid in the differentiation of mute, regressive psychotic-like reactions from actual psychoses. One patient produces a wealth of paranoid ideas, hallucinations, and the like, while another, with approximately the same clinical picture, hallucinates and relives the traumatic events which precipitated his symptoms. The prognosis is relatively good if the thought content, as determined by material released during abreaction, is concerned primarily with recent battle trauma (cases 1 to 5). With some patients, however, childhood or adolescent traumatic experience comes to the fore. For example, a catatonic-like patient who complained of pains in the shoulders and back, when abreacting began hallucinating his unexpectedly early return from elementary school, saw his mother in the midst of intercourse with a stranger on the living room floor, flung himself on his rival, felt his shoulder gripped and was hurled against the wall, bruising his back. This type of reaction is not uncommon and seems usually concerned with fantasied or actual sexual experience, not necessarily, as in this case, incestual. We believe that with such patients the fundamental mechanism is probably schizophrenic, rather than that of a major hysteria (case 7). For such patients, diagnostic abreaction is indicated, but abreactive therapy should be approached with infinite caution. It seems, in fact, contraindicated for most psychotic patients.

21. Hartman, J.: Unpublished data.

A few illustrative examples may be of value. Detailed case histories have been incorporated in various articles already published. This paper is concerned primarily with abreaction as such, and therefore no attempt will be made to present the detailed psychodynamics and developmental histories of the patients involved. All were in their middle twenties. All had had at least two months of combat. Several had been awarded medals for undoubted heroism. All were amnestic for the traumatic experiences which precipitated their symptoms. Unless otherwise stated, the precombat personalities were essentially stable. Therapy consisted primarily of ventilating conflict material on the conscious level. Within four to six weeks, sufficient insight was attained in each case, and enough of a psychologic reorientation effected, for us to describe the result as symptomatic recovery. All were transferred to the Zone of the Interior. For most, unfortunately, follow-up studies have not as yet been obtainable. The cases are summarized as follows:

CASE 1.—Spontaneous abreaction to noise. The patient was defecating by the side of a road when his tank was blown to smithereens and its crew killed. He immediately became amnestic for the whole incident and, as a result, was soon hospitalized, a jittery and tremulous patient with extreme sensitivity to noise, pronounced disturbance of sleep and terrifying combat nightmares. Treatment consisted of modified insulin and amytal narcosis. Within six weeks he was discharged to noncombat duty. While still hospitalized, he had had frequent "black-outs," as a result of which he had been specifically instructed to see no pictures except Mickey Mouse cartoons. Two days after his discharge to a replacement depot, his anxiety was pronounced enough to necessitate rehospitalization, and he was admitted to this installation. He seemed calm and well oriented; nevertheless, he was unable to remember what had happened. While we were taking his history, a door in the ward slammed shut. In an instant he was crouching in a corner of the room, his eyes widely dilated. His tank was again aflame! His comrades were being incinerated! Shells began falling round about! He started to shoot a sniper some distance away (and if he had actually had a gun, one of us would no longer be alive!). A plane swooped down, strafing the road! He rolled panic-stricken into a ditch, landed head first and lost consciousness. With this, the abreaction came to an end, eight or ten minutes after it had begun.

If this abreaction had occurred before the patient had been rehospitalized, it is possible that nearby property would have been damaged, persons hurt and medicolegal complications arisen. As it was, the patient knew only that another brief "black-out" had taken place. He was completely amnestic for both abreaction and incidents abreacted. Nevertheless, with material so close to the surface as this, aeration on the conscious level was indicated. Neither intravenous administration of barbiturates nor suggestion hypnosis was needed. He was therefore given three or four psychotherapeutic interviews a week during a four week period. The material became conscious; his previous patterns of behavior came to light; insight was attained, and a symptomatic recovery was effected.

CASE 2.—Spontaneous abreaction to discussion of combat by other patients. The patient, a private first class, after two and one-half months in the line was placed in noncombat service because of "combat exhaustion". He seemed unable to discharge even the mildest of duties with any acceptable degree of efficiency

and was therefore hospitalized, boarded and transferred to this installation for holding until his transfer to the states became effective. On his admission here, his affect seemed somewhat flat; he had difficulty in concentrating and complained of occasional combat nightmares. Aside from this, he seemed free from symptoms. Nevertheless, on the afternoon of his admission, when fellow patients began to reminisce about combat experience his eyes dilated, he began to tremble and he found himself back in combat again. This occurred three times during his first two days here, once on his fourth day in the hospital and once on his sixth. The stimulus was always the same. On each occasion his abreaction lasted three to five minutes. During his twelve days at this installation, he received seven hours of individual psychotherapy. His affect no longer seemed flat, and he stated that he no longer had difficulty in concentrating. So far as we could determine, he was free from symptoms at the time of his transfer to the Zone of the Interior.

CASE 3.—Spontaneous abreaction to discussion of combat by the patient himself. The patient was hospitalized for two and one-half months, after which he was discharged to noncombat duty only to be rehospitalized within a week. Two months later, or four and one-half months after his original breakdown, he was transferred to this installation, as a case of moderately severe anxiety with a pronounced startle reaction and complete amnesia for traumatic experiences immediately preceding his initial hospitalization. However, he had previously had four sessions of abreaction induced with pentothal and one induced with amytal. According to his statement, "I blew my top each time. The next day, the doc would tell me everything I said. That's how I know what happened. But I don't remember anything about it."

Free association was tried with this patient. Within five minutes he began describing his early combat experiences, and ten minutes later he was actually reliving them again. Abreaction was induced in this way on four successive days, and the abreacted material was discussed with him immediately after each session. The first two abreactions were characterized by amnesia for the events abreacted. The third was so pronounced that the very intensity of the emotional release "awakened" him, and abreacted material was recalled as though part of a nightmare. The fourth abreaction was remembered in detail. On the fifth attempt, this patient was able to discuss combat without hallucinating. Within a week, he seemed free from symptoms. For three weeks, however, he received three psychotherapeutic interviews a week, of from one-half to three quarters of an hour each. He was then transferred to the States, at the time of his discharge from this hospital, so far as we could determine, with a symptomatic recovery.

CASE 4.—Abreaction induced with barbiturates followed later by suggestion hypnosis. This patient's break had been precipitated in the Ardennes salient three months before he was transferred here as a catatonic type of dementia precox. During this period, he had apparently been almost motionless and completely mute. On occasion it would seem as though he were trying to speak, only to drool instead. His eyes usually seemed about to pop from his head. Occasionally he would play with toys like a 3 year old, and at such times his face would relax into a delightfully ingenuous childlike smile. Hypnosis was unsuccessfully attempted, and therefore abreaction was induced by intravenous administration of amytal. Strong suggestion was given toward the close of the session. Subsequent abreactions were induced with suggestion hypnosis. The patient incidentally had had a year of college psychology. When hypnotized, he stated in so many words that he was utilizing his symptoms as an escape from combat, that he had no desire to get well and that he wished we would let him alone. Nevertheless, despite

his rationalization about his symptoms, we can see no basis for considering the possibility of malingering.

The literature is replete with the case histories of patients successfully treated with abreaction. The following cases illustrate possibilities of failure of the type mentioned in the preceding discussion. For obvious reasons, brief developmental histories with some of the material released during the course of the abreaction are included as part of the illustrative material.

CASE 5.—Postabreactive amnesia for material abreacted. A 19 year old rifleman had stammered until the age of 5 and was afraid of high places but his past history was otherwise stable. After three and one-half months of continuous combat, he was hospitalized for three weeks because of a badly contused left knee, after which he was returned to duty, only to be rehospitalized five days later, stammering, tremulous and jittery. During the next six weeks his symptoms became progressively worse, and he was transferred to this installation. On his admission, his speech defect was no pronounced as to make him completely ununderstandable. He therefore found it necessary to write whatever he wished us to know. His heart was racing, and he had severe pain in the chest. He was depressed by thoughts of dead comrades, was plagued by nightmares of Germans throwing dismembered limbs at him before he bayoneted his tormentors, and was agonized by severe headaches. Sleep was difficult and at times impossible. He showed extreme sensitivity to noise. General information and intelligence were unimpaired.

During the course of his first abreaction, he described a bombing raid in the past tense. Then, "after it was over, I started shaking. I couldn't talk so good. That was all. . . . After that, we started to move. We . . . we . . . I . . . I don't know what the hell we were doing there, but we waited. And a sniper took a pot shot at me. I got scared. We looked around—couldn't see no one. I saw another sniper. He took a pot shot at my buddy. He hit him! I shot him out of the tree. He had his hand on his right arm. He started hollering, *'Kamerad!'* I said 'f——k him!' When he came up to me, I shot him 10 yards away. He didn't have a gun. . . . And I'm always trying to forget about it. He tried to shoot me. He killed my buddy. I couldn't save him. . . . And the f—king Germans were shooting machine guns at us. I saw a tracer coming right at me. I fell to the ground. . . . Get that bastard! Where's my gun? I got him! They're shelling! Stay in your hole, men! God dam them—that one was close. Down, men! Stay down! [Tears] He's killed! They've got him. He had a nice family back home. Two blocks away, we lived. Kill the bastards! . . . I'll shoot! I'll shoot them all! I've got that f—king son of a bitch! I bayoneted that other c.s. . . . I bayoneted him! I tried to forget him! I can't! I can't!" And this patient saw three and a half months of grueling infantry combat after this particular experience.

Soon after each abreaction, he would become amnestic for the events abreacted. The material was nevertheless discussed with him. By the time of his transfer to the Zone of the Interior, four weeks later, all but one of his symptoms had disappeared, but his stammer was still so pronounced as to make it impossible to understand anything he tried to say.

CASE 6.—Partial remission effected by electric shock, followed by abreaction-induced reprecipitation of original symptoms. The patient, a 19 year old private,

hated his father because the latter beat him and his mother. He had stammered until the age of 7, was enuretic and somnambulistic until he was 10 and frequently had ejaculatio precox. He had served through the African and Sicilian campaigns as a cannoneer. He was hospitalized with a moderate startle reaction. He was unable to eat or sleep, had hallucinations of the presence of dead comrades and was profoundly depressed and suicidal. After three electric shocks, he showed a partial remission. He was in contact, but the symptoms present on admission were reprecipitated when he underwent abreaction. Whether or not he would have had a relapse within a few days if abreaction had not been tried is impossible to state.

CASE 7.—Abreactive material not concerned primarily with combat experience. The patient was a 26 year old corporal whose background included a loveless marriage with a girl who two years later divorced him, a passionate love affair with another girl who became his mistress but refused to marry him because of differences in their respective religions, an intense ambition to become a writer and a legal education which he had not quite completed before his induction into the service. His break was precipitated during the collapse of the Ludendorf bridge. On admission, he was confused, wandered aimlessly about the ward, was constantly in a deep fog, seemed disoriented for time and place and was unable to remember his age or any details about his past life. Under suggestion hypnosis, he abreacted segments of his whole life in cross section, the individual events being tied together by the same emotional tone. A portion of the abreacted material follows. "He's up on the bridge. He's a human animal. I wish he were dead. I wish the bridge would cave in. . . . It's falling down! See what you did? See what happens to bad people? Can't torment me any more! See how you suffer? There's something the matter with my head. Whitie—he threw a rock at it. If he ever does that again, I'll hurt him. I won't have bad little boys coming into my kingdom. I won't let him climb and climb into the clouds with me. And you're a human animal, too. You say you won't marry me? You ought to be dead! I'll kill you! I'll kill you! I'll kill you all!"

We believe that in this case an underlying schizophrenic reaction type was asserting itself. The abreaction therefore can be considered a diagnostic one.

## SUMMARY AND CONCLUSIONS

Some of the more recent literature dealing with abreaction is discussed and reviewed, and illustrative cases are reported. The following conclusions are reached as the result of our experience with patients in the only general hospital in the European Theatre of Operations in which the total case load was continuously neuropsychiatric.

1. With some patients, abreaction can be induced spontaneously. Many abreactive agents are available, among them sodium amytal, pentothal, ether and nitrous oxide. We believe that suggestion hypnosis is the method of choice because of the ease of administration and the simplicity of technic. Most acute psychiatric combat casualties can be hypnotized as readily and as quickly as the abreaction can be induced with intravenously injected barbiturates. It is therefore recommended that the latter method be used only when suggestion hypnosis is unsuccessful.

2. Abreactive therapy seems of importance primarily as an initial step in the treatment of acute battle reactions with amnesia, severe anxiety symptoms, hallucinations, regressive phenomena or major conversion symptoms. It is believed to be of value because of the sometimes amazingly rapid symptomatic recoveries which it helps to effect. Such therapy, despite its frequent superficially dramatic, and even melodramatic, results, must be considered merely as part of a long range psychotherapeutic program designed to meet the needs of the individual patients under treatment. Other forms of psychotherapy must be utilized in addition or the patient will relapse. This is true because of the underlying relation of present symptoms, old neurotic conflicts, personality development and general patterns of behavior. Nevertheless, the value of emotional catharsis per se should not be minimized.

3. In the military setting, abreaction is contraindicated for the continued treatment of psychotic patients, for certain types of patients with pronounced startle reactions, for chronically neurotic persons and patients with hypochondriacal syndromes and for patients for whom repressive technics are indicated.

4. Abreaction may also be utilized with some patients for the differential diagnosis of psychoses from psychotic-like and neurotic reactions. With the latter, abreactive thought content for the most part seems concerned primarily with recent combat experience. It may also be utilized, but warily, for the differential diagnosis of malingering, provided it be kept in mind that malingering often constitutes a symptom.

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# NEUROGENIC ARTHROPATHY (CHARCOT JOINT) ASSOCIATED WITH DIABETIC NEUROPATHY

## Report of Two Cases

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IT is a matter of general knowledge that tabes dorsalis or syringomyelia underlies most neuropathic joints; the mechanism by which these diseases predispose afflicted persons to the development of neurogenic arthropathy (Charcot joint) is still imperfectly understood. Disease processes which afflict areas of the nervous system other than those involved in tabes dorsalis or syringomyelia offer an approach to a better understanding of the genesis of such joint disorders; for this reason, and because of the scarcity of similar observations, the following cases of Charcot joint complicating the neuropathy of diabetes mellitus are presented.

### REPORT OF CASES

CASE 1.—*History.*—W. E., a poolroom proprietor aged 23, was admitted to University Hospital because of swelling of the left foot, of five months' duration. His occupation required him to stand about ten hours a day, and for two or three months prior to onset of the swelling he had worn canvas shoes with thin rubber soles instead of his customary firm leather shoes but no specific trauma to the foot was recalled. The swelling increased with activity and subsided somewhat with elevation of the foot; there had been mild pain in the calf at the onset but none in the area of swelling. There was no redness, drainage, previous abrasion of the skin, fever or constitutional symptoms.

Polyuria, polydypsia, polyphagia, glycosuria, loss of weight and enuresis began at the age of 13 years; insulin and dietary therapy was instituted and closely supervised for the next three years, with relative freedom from symptoms. Less care was exercised in the management of his diabetes during the next four years, but no complications appeared except for numbness in the legs at the age of 20. When he was 21, acidosis without coma had developed, and the diet and insulin dosage were readjusted. At the age of 22 all use of insulin was discontinued for one month in order to try an oral therapy for diabetes; he lost 30 pounds (13.6 Kg.) in one month and again experienced acidosis but regained weight and strength after the institution of insulin therapy and a restricted diet.

For three years he had noted numbness of both legs below the knees, and for six months he had urinated only once or twice daily. Erections and ejacu-

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lations were normal. He stated that he had been generally weak in both the upper and the lower extremities since the diabetes was first discovered, with less muscular strength than the average throughout his later development; but there had been no noticeable change in recent years except when he had acidosis.

There was no history of syphilis. His father, mother, sibling (1), wife and 4 month old daughter were living and in good health.

*General and Neurologic Examination.*—Punctate retinal hemorrhages were present bilaterally. The left forefoot showed moderate edema and induration over the midtarsal area, loss of the longitudinal arch and painless hypermotility, with slight crepitus on passive motion. The pulsations of the dorsalis pedis and posterior tibial arteries were easily palpable.

The cranial nerves were normal. There were mild diffuse weakness of the extremities, with generalized flabbiness and hypotonia, and focal diminution in muscular power in the dorsiflexors of the left ankle, apparently due to the local bony lesion. Fibrillations, focal atrophy and ataxia were absent. The biceps, triceps, patellar, hamstring and achilles reflexes were absent and the plantar reflex was diminished bilaterally. The abdominal and cremasteric reflexes were normal. Vibratory sensation was slightly diminished distally in the lower extremities; deep pain sensibility and the sense of position were well preserved. Superficial pain sensation was absent in a stocking fashion from 3 inches (7.5 cm.) above the malleoli distally and was diminished to 2 inches (5 cm.) below the patellas, the loss being slightly greater on the right than on the left. Temperature sensation was absent from 2 inches above the knee bilaterally and was diminished to the groins; tactile sensation was absent over the toes and was diminished to the knees. Sensation was normal over the saddle area, the trunk and the upper extremities. Tenderness of the muscles and nerve trunks was absent. Cystometric examination revealed an early atonic neurogenic bladder (first desire to void at 250 cc.; maximum intravesical pressure, 6 mm. of mercury; capacity, 800 cc.; doubtful temperature perception, and no residual urine). Sweating tests showed normal sweating over the abdomen and groin, diminished sweating over the thighs and absence of sweating from 1 inch (2.5 cm.) above the knees distally. Cutaneous temperature recordings were taken at constant room temperatures with the patient in the resting state, after use of nicotine, after immersion of the arms in hot and cold water and after spinal anesthesia used to give a complete sympathetic block. The resting temperature over the dorsum of the left foot consistently averaged from 2.25 to 2.75 degrees (C.), or 4.05 to 4.95 degrees (F.), higher than that over the right foot; after the use of nicotine the cutaneous temperature increased (normally decreases) over both feet. After spinal block the cutaneous temperature increased only 1.07 degree (C.), 1.92 degrees (F.), over the left foot and 1.37 degrees (C.), or 2.66 degrees (F.), over the right foot (average increase in normal persons from 5 to 9 degrees (C.), or 9 to 16.8 degrees (F.). The distal reduction in temperature commonly present with peripheral vascular disease was not observed. The findings were interpreted as those of partial paralysis of the vasoconstrictor fibers to the lower extremities, the paresis being greater on the left than on the right.

*Laboratory Examinations.*—Glucose and acetone bodies were present in the urine on his admission to the hospital. The hemoglobin of the blood measured 15.6 Gm.; the red cell count was 5,200,000 and the white cell count 5,000, per cubic millimeter and the differential count was normal. Roentgenographic examination of the chest was normal, and the test with tuberculin gave a negative reaction. The sedimentation rate was normal. The dynamics of the cerebro-

spinal fluid were normal; the cellular content was 4 per cubic millimeter. The Pandy reaction was positive for globulin, and the total protein measured 74 mg. per hundred cubic centimeters. The colloidal gold curve was 0000000000, and the Kahn reactions of the blood and cerebrospinal fluid were negative. Roentgenograms of the spine revealed minimal spina bifida occulta of the first sacral segment; roentgenograms of the left foot (fig. 1) showed extensive disorganization of the tarsometatarsal joints. There was advanced destruction of the three

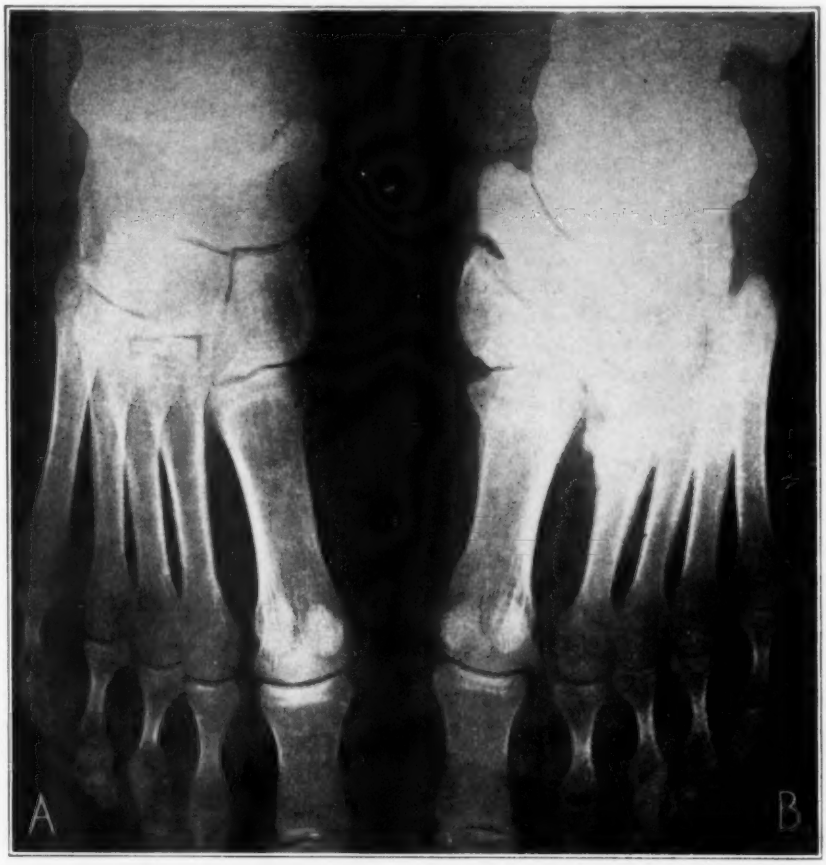


Fig. 1 (case 1).—*A*, normal right foot; *B*, neuropathic tarsal joint of the left foot, with medial displacement of the cuboid and navicular bones, destructive changes in the tarsal and metatarsal bones, loss of the joint surfaces and proliferative changes, best seen about the metatarsal heads of this projection.

cuneiform bones and their adjacent surfaces; the cuboid and navicular bones were displaced medially. The medial and distal surfaces of the cuboid bone, the distal surface of the navicular bone and the proximal ends of the second, third and fourth metatarsal bones were involved in the destructive process. Proliferative changes were present in the metatarsal heads, and there were numerous loose bodies about the area of disorganization. No change could be seen in roentgenograms made one month later.

*Course.*—On a diet furnishing 3,000 calories per day and containing 100 Gm. of protein and 200 Gm. of carbohydrate, the patient was rendered aglycosuric with 40 units of protamine zinc insulin and 65 units of regular insulin daily.

CASE 2.—*History.*—G. W., a farmer aged 29, single, was admitted to the University Hospital because of painless, progressive swelling and deformity of the left ankle, appearing without apparent precipitating cause two months prior to examination. He had continued to bear his weight on the foot until an ulcer developed over the lateral malleolus, five weeks after onset.

At the age of 12, after a six month period of polyuria, polydypsia, polyphagia and loss of weight, the patient passed into coma and a diagnosis of diabetes mellitus was made. For two years treatment with insulin and a high fat diet was carried out; then use of insulin was discontinued for four years, although the prescribed diet was followed. At the age of 18 a higher carbohydrate diet with insulin was prescribed, but periodic urinalyses usually showed some degree of glycosuria. At the age of 22, after a period of loss of weight, he was told by a physician that he was in acidosis. Shortly thereafter a minor abrasion of the anterior surface of the left leg led to a severe infection, requiring surgical drainage and six weeks of hospital treatment. Irregular amounts of insulin were used in the following two years, and an ulcer developed under the base of the right great toe. Large amounts of sugar were present in the blood and urine on admission to the hospital at this time, and ten weeks of hospital care was required to control the diabetes and to heal the ulcer. At the age of 27 the second toe of the left foot became infected and amputation was necessary. More care was taken with the diet and administration of insulin in the ensuing two years, but some degree of glycosuria persisted.

Numbness and tingling in the hands and feet had been present about three years; cramps occurred frequently in the calves. He did about one-half an average farmer's duties per day because of weakness and ease of fatigue. He urinated but once or twice daily and had never had erections or ejaculations.

There was no history of syphilis; the father had died of cancer of the throat and the mother of diabetes. There were no siblings.

*General and Neurologic Examination.*—Linear and punctate retinal hemorrhages were present bilaterally. The liver descended 3 cm. below the costal margin on inspiration. The scars of surgical drainage were present over the anterior and lateral aspects of the middle third of the left tibia, and a clean, graulating ulcer was present over the inferior portion of the lateral malleolus. Induration and edema extended midway up the tibial surface of the left leg; there were painless hypermotility, crepitus on passive motion and pronounced medial displacement of the left ankle. The toe nails were brittle, and the skin over the legs was dry and scaling. The second toe on the left foot had been amputated (fig. 2). The pulsations of the dorsalis pedis and posterior tibial arteries were palpable.

The cranial nerves were normal. There were mild diffuse muscular atrophy, hypotonia and paresis of the upper and lower extremities bilaterally, with somewhat greater paresis of the extensor hallucis longus muscles. Voluntary motion of the left ankle was impaired because of the derangement of the joints. Fibrillations, focal atrophy and ataxia were absent. The biceps and patellar reflexes were weakly preserved bilaterally, and the abdominal reflexes were normal. The triceps, cremasteric, hamstring and achilles reflexes were absent, and the plantar reflexes were diminished. Vibratory sensation was diminished distally in the lower extremities; the sense of position was intact. Deep pain sensibility was

diminished in the achilles tendon, the hamstring tendons and the testis on both sides. Superficial pain sensibility was absent below the midcalf on the left, approximating a stocking type of sensory loss, and was diminished to about 3 inches below the inguinal ligament; it was absent from 1 inch above the malleoli distally of the right leg and was diminished to the level of the knee. Temperature sensation was impaired over a similar distribution, the loss likewise being greater on the left side than on the right. Tactile sensibility showed a minimal distal diminution below the malleoli bilaterally. There was no disturbance in sensation in the saddle area, the trunk or the upper extremities. Tenderness over the muscles and nerve trunks was absent. Cystometric examination showed an atonic neurogenic bladder (first desire to void at 400 cc.; maximum intravesical pressure, 4 mm. of mercury; capacity, 1,500 cc.; absence of temperature

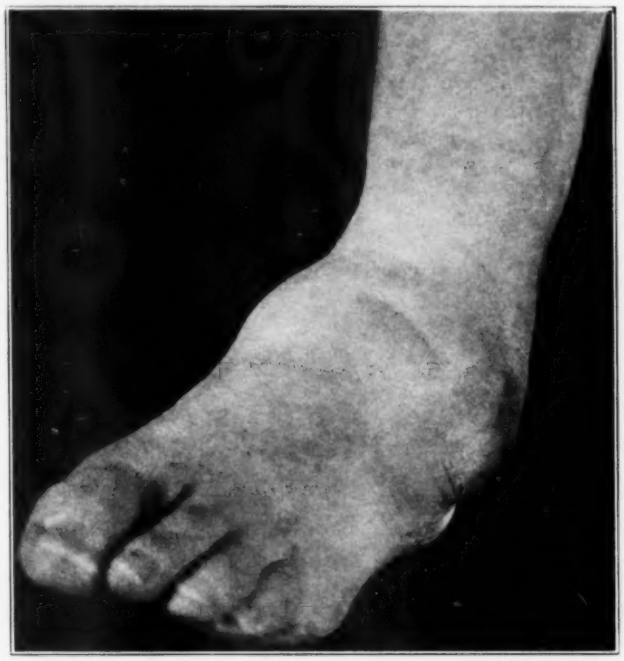

Fig. 2 (case 2).—Edema and displacement of the left ankle, dry hyperkeratotic skin and ulcer over the lateral malleolus.

perception, and 80 cc. of residual urine). Sweating tests showed normal sweating responses over the thorax, abdomen and groin; slight diminution over the lower third of the lateral aspect of each thigh, and complete symmetric absence of sweating from 1 inch below the knees distally. The results of cutaneous temperature recordings were interpreted as those of almost complete symmetric paralysis of the vasoconstrictor fibers to the lower extremities. There was no local increase in heat over the afflicted joint; the disturbance was symmetric, and it was of greater magnitude than that in case 1. The characteristic cutaneous temperature readings of occlusive peripheral vascular disease was not found.

*Laboratory Examinations.*—In addition to glycosuria, urinalyses revealed a constant 2 plus reaction for albumin, without casts or red blood cells. The hemoglobin of the blood measured 12.4 Gm., and there were 8,600 white blood

cells per cubic millimeter. The sedimentation rate was normal. The Kahn reactions of the blood and the cerebrospinal fluid were negative. The dynamics of the cerebrospinal fluid were normal; the cells numbered 6 per cubic millimeter. The Pandy and Nonne-Apelt reactions for globulin were positive; the total protein content was 160 mg. per hundred cubic centimeters, and the colloidal gold curve was 0000000000. Roentgenograms of the gastrointestinal tract showed 15 per cent gastric retention at the end of five hours and impaired motility in the small

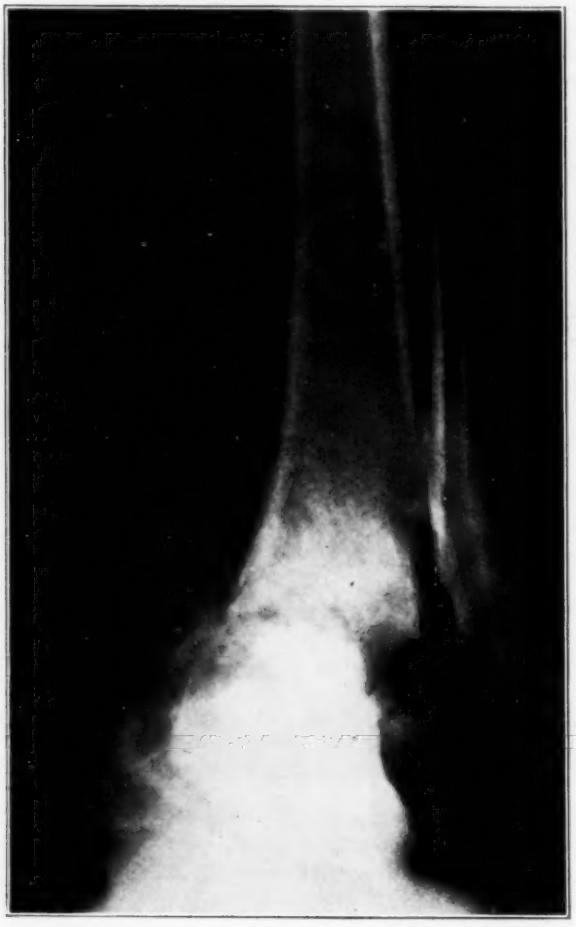

Fig. 3 (case 2).—Neuropathic left ankle joint, with medial displacement of the left ankle, destructive changes in the tibia, fibula and astragalus and loose calcium bodies surrounding the astragalus.

intestine. Roentgenograms of the spine, the pelvis and the right leg were normal. On the left side (fig. 3) there was severe disorganization of the ankle joint. The normal articulations of the astragalus with the tibia, fibula and os calcis had disappeared, with loose bodies above and about the remnants of the astragalus. The distal portion of the fibula had slipped downward from its articulation with the astragalus, and the ankle joint was displaced medially. The navicular bone,

os calcis and distal portions of the tibia and fibula showed loss of substance and fragmentation at their articulation with the astragalus.

*Course.*—On a diet furnishing 2,600 calories per day and containing 90 Gm. of protein and 200 Gm. of carbohydrate, the patient was rendered aglycosuric with 40 units of protamine zinc insulin and 30 units of regular insulin daily.

The foot was placed in a well padded shoe with a rigid caliper brace, and the diabetes was maintained under excellent control on the aforestated regimen. He

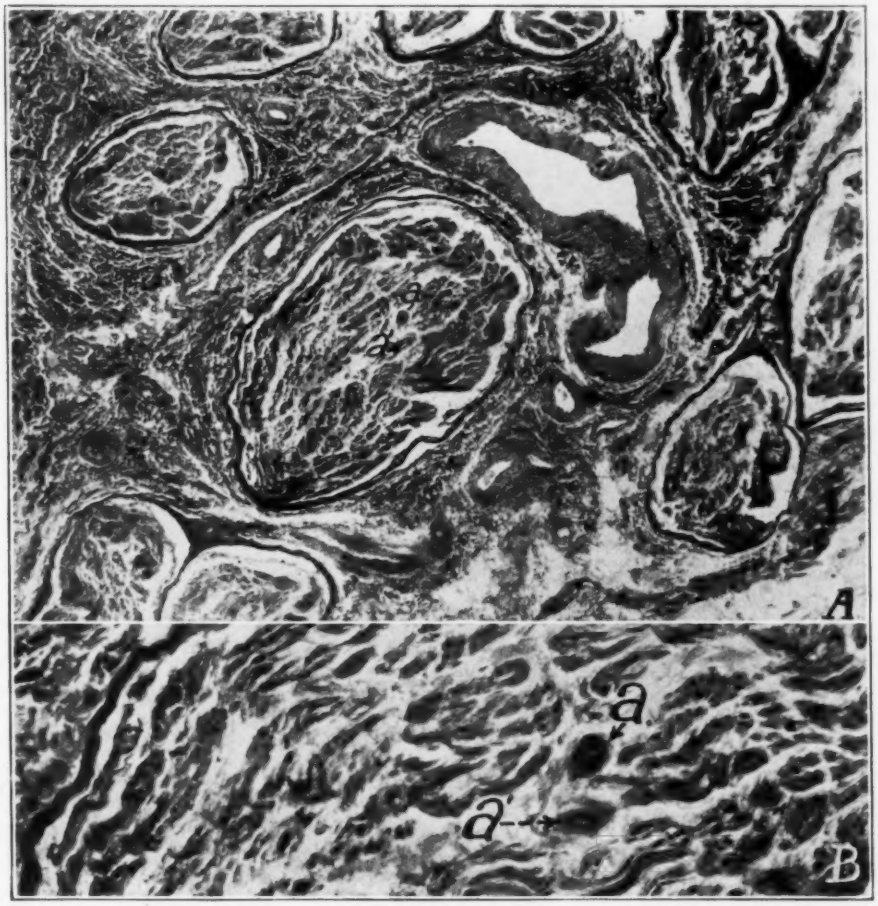


Fig. 4 (case 2).—*A*, posterior tibial nerve, showing advanced perineural fibrosis, endoneural fibrosis and hyalinization of the endoneural arterioles at *a* and *a'*. Hematoxylin and eosin stain; × 70; United States Army Medical Museum negative no 91819. *B*, higher magnification (× 230) of a portion of the same section. United States Army Medical Museum negative no. 91814.

was reexamined at regular intervals; although the ulcer never showed any gross signs of infection, no healing occurred over a period of two years. There was no appreciable change in the neurologic status, and no striking changes appeared in serial roentgenograms of the ankle.

Twenty-five months after the patient was first seen, a guillotine amputation through the midcalf was performed, followed by plastic repair of the stump.

The wound healed uneventfully; a prosthesis was fitted, and the stump adjusted well to weight bearing. When the patient was last seen, the diabetes was under control with 90 units of insulin daily and a diet of 3,000 calories per day, containing 110 Gm. of protein and 200 Gm. of carbohydrate.

*Pathologic Study.*—Examination of the tissue removed by amputation showed severe degenerative changes in the peripheral nerves (fig. 4). There were striking reduction in the myelin sheaths and axis-cylinders, an increase in Schwann cells and advanced endoneural and perineural fibrosis; the smaller arterial branches within the nerve bundles had undergone varying degrees of hyaline degeneration. The arteries throughout the specimen showed mild to moderate hyalinization of their walls; one branch of the posterior tibial artery contained an old, well organized thrombus, which had recanalized. The malleolar ulcer had a base of

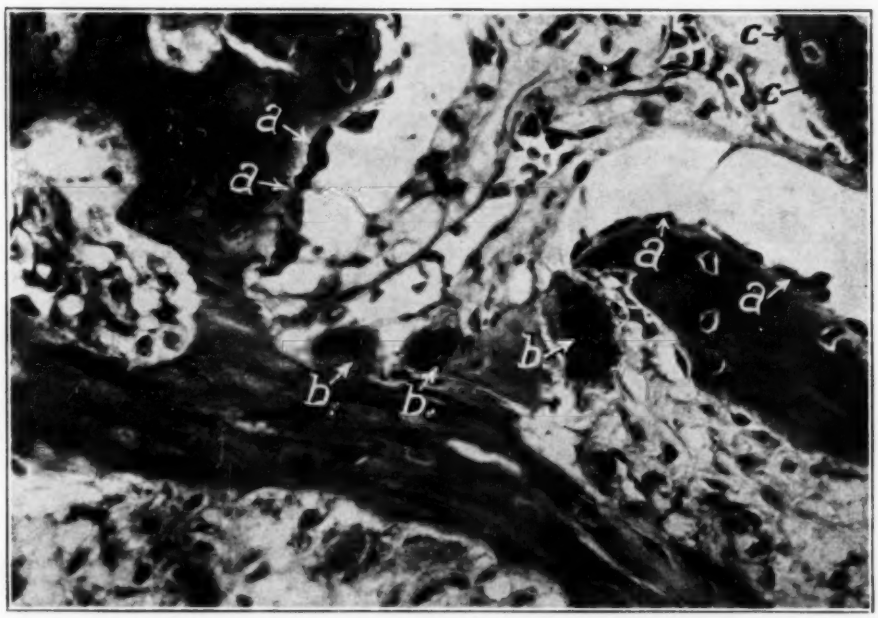


Fig. 5 (case 2).—Osteoblastic activity (*a*), adjacent to osteoclasts (*b*), and areas of bone resorption (*c*). Left astragalus; hematoxylin and eosin stain; × 500; United States Army Medical Museum negative no. 91816.

vascular granulation tissue, and there was pronounced hyperplasia of the marginal stratified squamous epithelium. The bone marrow (fig. 5) was fibrotic; areas of vascular granulation tissue with lymphocytes and plasma cells replaced the bone marrow in some regions. Signs of new bone formation were evident in many areas, frequently adjacent to regions undergoing bone resorption.

## COMMENT

Sensory disturbance, areflexia, predilection for the lower extremities, minimal or no muscular atrophy and paresis and minimal or no tenderness over the nerve trunks and muscles are the generally recognized features of chronic diabetic neuropathy [1] and were present in both these

cases. The presence of poorly regulated diabetes of ten and seventeen years' duration, respectively; the pattern of neurologic changes; the absence of historical, clinical or serologic evidence of syphilis, and the absence of distinctive signs of lumbosacral syringomyelia are compatible, we believe, with the diagnosis of chronic diabetic neuropathy complicated by Charcot joint; the pathologic changes of chronic neuropathy and neuropathic disease of bone corroborate the clinical diagnosis in case 2.

Within the limitations inherent in a clinical analysis, the lesions would appear to be predominantly extramedullary, with the major involvement in the posterior roots, the posteror root ganglia and the sensory components of the peripheral nerves and with relative sparing of the ventral roots and the motor fibers of the peripheral nerves. A high concentration of protein in the spinal fluid is characteristic of the Guillain-Barré type of radiculoneuritis, in which there are anatomic changes in the posterior roots and posterior root ganglia;[2] its presence in these cases is evidence of radicular localization. The localization of the lesions responsible for the disturbed function of the autonomic nervous system (decrease in gastrointestinal motility, decreased sweat secretion over the legs, disturbed vasomotor reactions in the legs, disturbance in vesical muscle tone) is less precise, but an extramedullary origin seems most probable. Dees and Langworthy[3] produced atonic neurogenic bladders in animals by section of the posterior roots of the second, third and fourth sacral spinal nerves. Bayliss,[4] Foerster[5] and others[6] showed that stimulation of the distal end of divided posterior roots causes peripheral vasodilatation. The sudomotor fibers concerned

1. Wilson, S. A. K.: Neurology, Baltimore, Williams & Wilkins Company, 1940, page 300. Woltman, H. W., and Wilder, R. M.: Diabetes Mellitus: Pathologic Changes in the Spinal Cord and Peripheral Nerves, Arch. Int. Med. **44**:576-603 (Oct.) 1929.

2. Löwenberg, K., and Foster, D. B.: Polyradiculoneuritis with Albuminocytologic Dissociation: A Pathoanatomic Report of Three Cases, Arch. Neurol. & Psychiat. **53**:185-190 (March) 1945.

3. Dees, J. E., and Langworthy, O. R.: An Experimental Study of Bladder Disturbances Analogous to Those of Tabes Dorsalis, J. Urol. **34**:359-371 (Nov.) 1935.

4. Bayliss, W. M.: On the Origin from the Spinal Cord of the Vasodilator Fibers of the Hind-Limb, and on the Nature of These Fibers, J. Physiol. **26**:173-209, 1901.

5. Foerster, O.: Ueber die Vasodilatatoren in den peripheren Nerven und hinteren Rückenmarkswurzeln beim Menschen, Deutsche Ztschr. f. Nervenh. **107**:41-56, 1928.

6. Zuckerman, S., and Ruch, T. C.: Spinal Roots and Tracts in the Regulation of Skin Temperature, Am. J. Physiol. **109**:116-117, 1934. Toennies, J. F.: Conditioning of Afferent Impulses by Reflex Discharges over the Dorsal Roots, J. Neurophysiol. **2**:515-525 (Nov.) 1939.

in thermoregulatory sweating are known to follow the peripheral course of sensory nerves;[7] no constant change in sweating follows posterior rhizotomy.[8]

Evidence of disturbance of the autonomic nervous system associated with the neuropathic joints of syringomyelia was presented by Dreyfus and Zarachovitch,[10] who found local arterial vasodilatation by oscillometric examination over the foot of a patient with syringomyelia who had multiple spontaneous fractures of the tarsal bones. Wartenberg[11] cited no specific cases but stated that elevation of the local temperature, rise in the arterial and venous blood pressures, increase in the oscillometric index, anomalies of sweat secretion and disturbances in the pilomotor reflex were found in the neighborhood of the neuropathic joints of tabes. Disturbances in the vasomotor reactions of the feet analogous to those in our pateints were found in cases of peripheral neuritis by Wilkins and Kolb,[12] who used cutaneous temperature recordings in their investigation.

Charcot joint occurring with lesions of the peripheral nerves is of relatively infrequent occurrence as compared with its incidence in cases of tabes dorsalis and syringomyelia. The review of Shands[13] contains references to a number of such cases and describes the appearance of a Charcot ankle joint following a traumatic-infectious neural lesion. The condition has been described in association with tumors of the peripheral nerves, traumatic avulsion of nerves, callus formation from fracture constricting nerves and the neuritides of lead and leprosy. Jordan[14] mentioned the occurrence of a Charcot joint with diabetic neuropathy. Bailey and Root[15] reported painless destruction of the

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7. List, C. F., and Peet, M. M.: Sweat Secretion in Man: II. Anatomic Distribution of Disturbances in Sweating Associated with Lesions of Sympathetic Nervous System, Arch. Neurol. & Psychiat. **40**:27-43 (July) 1938.

8. List, C. F.: Personal communication to the authors.

9. Footnote deleted by the authors.

10. Dreyfus, G., and Zarachovitch: Gros orteil d'apparence syringomyélique avec fractures spontanées multiples du métatarse: Considérations physiopathologiques et therapeutiques, Bull. et mém. Soc. méd. d. hôp. de Paris **53**:328-333 (March 8) 1937.

11. Wartenberg, R., in discussion on Haldeman, K. O., and Soto-Hall, R.: Neuropathic Joint Disease, J. A. M. A. **111**:2043-2044 (Nov. 26) 1938.

12. Wilkins, R. W., and Kolb, L. C.: Vasomotor Disturbances in Peripheral Neuritis, Am. J. M. Sc. **202**:216-221 (Aug.) 1941.

13. Shands, A. R., Jr.: Neuropathies of the Bones and Joints: Report of Case of Arthropathy of Ankle Due to Peripheral Nerve Lesion, Arch. Surg. **20**: 614-636 (April) 1930.

14. Jordan, W. R.: Effect of Diabetes on the Nervous System, South. M. J. **36**:45-49 (Jan.) 1943.

15. Bailey, C. C., and Root, H. F.: Neuropathic Joint Lesions in Diabetes Mellitus, J. Clin. Investigation **21**:649 (Sept.) 1942.

joints of the tarsus in 14 patients with chronic, poorly controlled diabetes mellitus; they expressed the belief that the lesions of the joints were of a neuropathic type and were not dependent on syphilis, syringomyelia or deficient blood supply. The frequent coincidence of mal perforant and Charcot joint makes for a difficult differentiation from cutaneous infections of the feet with secondary osteomyelitis, and it is probable that neuropathic joints in the feet are associated with diabetic neuropathy more often than the scarcity of reports would lead one to believe.

None of the proposed theories of the pathogenesis of neuropathic joint has escaped criticism. The trophic theory of Charcot [16] would find considerable support if neuropathic joints could be shown to occur with isolated lesions of the autonomic nervous system. Neuroarthropathies were not observed in a series of 30 patients in University Hospital who were subjected to lumbar ganglionectomy for peripheral vascular disease, and reports of such occurrences have not been found in the literature. The analogy in this series is not an ideal one because of the regeneration of sympathetic fibers following surgical extirpation and the coexisting vascular disease; but there was a precise anatomic localization of the nerve lesion, it was limited to the sympathetic nervous system and the patients were carefully observed for long periods, some for as long as fifteen years. Corbin and Hinsey [17] failed to find any neuropathic changes in the bones or joints in cats under observation for three years following lumbar sympathectomy and section of the posterior roots. The presence of neuropathic joints in cases of nonsyphilitic diseases excludes Virchow's explanation of syphilitic osteochondritis. A humoral mechanism to explain the increased susceptibility of denervated joints to trauma was proposed by Katsuki,[18] who found that the parenteral administration of parathyroid extract or calcium chloride and the oral ingestion of sucrose facilitated the experimental production of Charcot joint in rabbits and dogs whose legs were traumatized after section of the posterior roots. Other corroborative evidence for this theory is so far lacking. Volkmann expressed the belief that repeated injuries to anesthetic joints were responsible for the development of Charcot joint; Turney,[19] who alleged that leprosy was the

16. Charcot, J. M.: Sur quelques arthropathies qui paraissant d'épendre d'une lesion du cerveau ou de la moelle épinière, Arch. de physiol. norm. et path. **1**:161, 1868.

17. Corbin, K. B., and Hinsey, J. C.: Influence of the Nervous System on Bones and Joints, Anat. Rec. **75**:307-319 (Nov.) 1939.

18. Katsuki, S.: Beitrag zur experimentellen neuropathischen Arthropathie und zugleich zu deren Pathogenese, Ztschr. f. klin. Med. **130**:567-574, 1936.

19. Turney, H. G.: Neurotrophic Affections of Bones and Joints, in Allbutt, C., and Rolleston, H. D.: System of Medicine, New York, The Macmillan Company, 1910, vol. 7.

only disease of the peripheral nerves responsible for Charcot joints, explained their presence in that disease by the chronicity, the analgesia of the deep tissues and the unimpaired muscular power, factors also present in tabes and syringomyelia. Eloesser [20] stated:

> Of three animals whose joints were subjected to operative trauma after having been previously rendered anesthetic by resection of posterior roots, all developed Charcot lesions. Trauma in a limb rendered anesthetic and analgesic experimentally leads to grotesque lesions of the bones and joints, which are in every way the counterparts of tabic fractures and arthropathies; trauma and lack of the warning sense of pain are the cause of most tabic bone and joint lesions.

Why the removal of the afferent impulses subserving the experience of pain and the trauma of normal weight bearing should produce such devastating lesions in the joints is not clear, although in recent years this "mechanical" theory has overshadowed the original Charcot theory of their genesis.

Since dysfunction of the autonomic nervous system appears to be associated with Charcot joint in those cases in which functional tests have been carried out, it seems premature to discard entirely the excellent clinical observations and deductions of Charcot because of his use of the term "trophic" and his inability to specify the anatomic pathway by which "trophic" functions were controlled. The factors common to most neuropathic joints are (1) trauma, from repeated small injuries, continued movement of a diseased limb or an isolated major trauma; (2) intact motor power to the afflicted joint; (3) impairment of afferent pain impulses; (4) diminution or absence of afferent proprioceptive impulses which normally inhibit hypermotility of joints; (5) chronicity of the underlying nervous disorder, and (6) metabolic disturbances, conditioned by hypotonic arteries and a defective temperature-regulating mechanism. A combination of these offers a more reasonable explanation for their development than either isolated metabolic or mechanical factors. This explanation, proposed in slightly different form by Wartenberg, is also in keeping with the pathoanatomic background of the disorders in which Charcot joint occurs, so far as they are known. In syringomyelia, cavitation with gliosis occur within the spinal cord in a location which permits interruption of visceral afferent and visceral efferent fibers in the intermediolateral cell column of the dorsal and lumbar portions of the cord, as well as interrupting the decussating fibers for pain and temperature of the ventral commissure. In tabes dorsalis and in the experimentally produced Charcot joint of Eloesser and Katsuki, the visceral afferent and vasomotor fibers of the posterior roots are interrupted, in addition to afferent somatic sensory stimuli.

20. Eloesser, L.: On the Nature of Neuropathic Affections of Joints, Ann. Surg. **66**:201-208 (Aug.) 1917.

A complete and entirely satisfactory pathologic description of the dorsal root area in cases of diabetic neuropathy is not available, but both Schweiger [21] and Williamson [22] described degeneration of the intramedullary fibers of the posterior roots and sclerosis of the posterior columns secondary to extramedullary lesions and likened the changes to those of mild tabes dorsalis.

SUMMARY

Two cases of severe, poorly regulated diabetes mellitus of ten and seventeen years' duration, respectively, are described. They were characterized by signs of damage to the somatic and autonomic nervous systems in the region of neuropathic joints of the lower extremities. From their functional and pathoanatomic analogy to the Charcot joint of tabes and syringomyelia and to experimentally produced Charcot joint in animals, it is suggested that dysfunction of the autonomic nervous system is of significance in predisposing the skeletal system to an overreaction to trauma, with the corresponding development of Charcot joint.

University Hospital, Ann Arbor, Mich.

21. Schweiger, L.: Ueber die tabiformen Veränderungen der Hinterstränge biem Diabetes, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **14**:391-405, 1908.

22. Williamson, R. T.: Changes in the Spinal Cord in Diabetes Mellitus, Brit. M. J. **1**:122, 1904.

# METASTASES OF UTERINE CARCINOMA TO THE CENTRAL NERVOUS SYSTEM

## A Clinicopathologic Study

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AND
CHARLES DAVISON, M.D.
NEW YORK

METASTASES of carcinoma of the uterus to the central nervous system are infrequent. These metastases are often solitary and may occur in the absence of widespread metastatic disease. In cases of a single metastatic nodule in the brain without evidence of carcinomatosis, the advisability of neurosurgical intervention should be considered, for in selected cases life may be prolonged appreciably by operation.

Three cases of metastatic brain tumor from uterine cancer, in all of which the primary growth was adenocarcinoma of the fundus, were studied pathologically at the Montefiore Hospital in the past twenty years. Because of the infrequency of such cases, they are reported here.

### REPORT OF CASES

CASE 1.—M. P., a housewife aged 46, entered this hospital in January 1928, with the complaints of convulsive seizures, some of which were right sided, weakness of the left side of the body, apathy, diplopia and headache. A carcinoma of the body of the uterus had been removed one year previously. The patient was right handed.

General physical examination revealed nothing significant except for tenderness over the right frontal region and over the lower part of the distended abdomen.

Abnormal findings on neurologic examination were mild nominal aphasia and acalculia, early bilateral papilledema, right homonymous upper quadrant visual field defects, weakness of right lateral gaze, inability to look upward, hemiparesis and hyperreflexia on the left side and a Babinski sign on the left.

Laboratory studies, which included roentgenographic examination of the skull, but not lumbar puncture, gave normal results.

After hospitalization, the patient became semistuporous; left hemiplegia developed, and she died suddenly on the twenty-third day of hospitalization.

*Autopsy.*—The diagnosis was: (1) status following hysterectomy for carcinoma of the uterus and (2) metastases of adenocarcinoma to the retroperitoneal lymph nodes and the brain.

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From the Neuropathological Laboratory and Neuropsychiatric Division of the Montefiore Hospital, and the Neurological Department of Columbia University College of Physicians and Surgeons.

Gross examination of the brain revealed a solitary, hard, yellowish tumor of the left frontal lobe (fig. 1). The microscopic diagnosis was metastatic adenocarcinoma (fig. 2). The spinal cord was normal in gross and microscopic appearance.

*Comment.*—Signs and symptoms of a neoplasm in the left temporoparietal region appeared one year after a hysterectomy for adenocarcinoma of the body of the uterus. The left hemiparesis was a false localizing sign and was probably due to compression of the right cerebral peduncle against the tentorium. Whether the patient's cerebral tumor was metastatic, rather than primary, could only be speculated on during life.

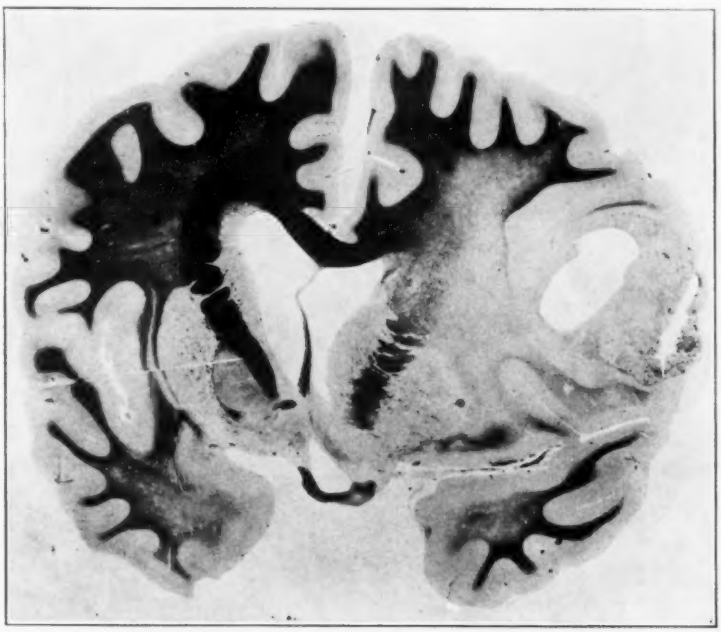

Fig. 1.—Circumscribed solitary metastatic nodule in the left hemisphere. Myelin sheath stain; × 1.

This case illustrates that carcinoma of the uterus may give rise to a solitary metastasis to the brain in the absence of metastases to other organs.

Case 2.—R. M., a woman aged 63, entered this hospital in October 1941, five years after panhysterectomy for adenocarcinoma of the body of the uterus (fig. 3). Her complaints on admission were loss of weight, cough with hemoptysis and enlarged suproclavicular lymph nodes.

General physical examination revealed nothing abnormal except for enlarged supraclavicular lymph nodes and signs of fluid in the right side of the chest. Neurologic examination showed a normal condition, but there was no record in the patient's chart that specific tests for cerebellar dysfunction had been made.

Laboratory data were noncontributory except for the roentgenologic confirmation of fluid in the right side of the chest.

The patient became progressively more dyspneic and died three months after admission. At no time did she have neurologic signs or symptoms.

*Autopsy.*—The diagnosis was: (1) status following hysterectomy and bilateral salpingo-oophorectomy for adenocarcinoma of the uterus; (2) metastases of adenocarcinoma to the lungs, pleura, lymph nodes, adrenal glands, kidneys, esophagus and brain, and (3) bilateral pleural effusion with bronchopneumonia and hemorrhagic infarct of the upper lobe of the right lung.

The brain on gross examination was normal except for a single, soft tumor, 3.5 by 1.75 cm. in size, involving the lobulus anterior and lobulus simplex of the

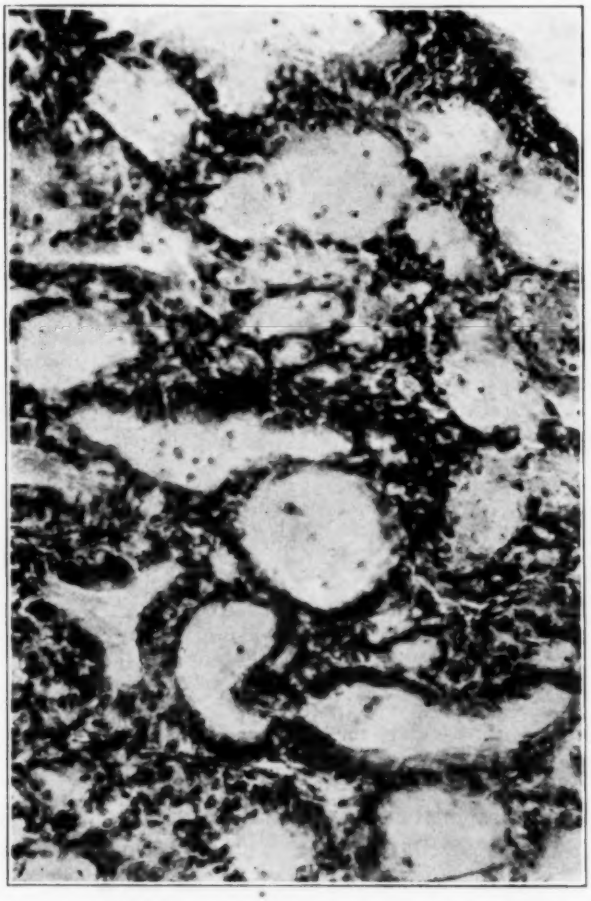

Fig. 2.—Adenocarcinomatous appearance of metastatic tumor of the central nervous system. Hematoxylin and eosin stain; × 100.

right cerebellar hemisphere (fig. 4). Microscopically the tumor was a metastatic adenocarcinoma (fig. 5), of the same appearance as the primary uterine carcinoma.

*Comment.*—Evidence of carcinomatosis appeared five years after the patient had a hysterectomy for a uterine adenocarcinoma. Although there were multiple metastases to many organs, only a single metastatic nodule was observed in the brain.

Case 3.—F. N., housewife aged 41, who had had a total hysterectomy for uterine adenocarcinoma five years previously, entered this hospital in April 1927 because of pain and weakness of the left lower extremity and loss of weight.

The abnormal findings on general physical examination were cachexia, enlarged cervical lymph nodes and moderate hepatomegaly.

On neurologic examination, the patient was found to be hyperemotional and slow in thought, with poor memory and judgment. Speech was slurred. The optic disks were pale; the tongue was deviated to the right, and there was right hemiparesis. Tendon reflexes were present and equal on the two sides except for a diminished

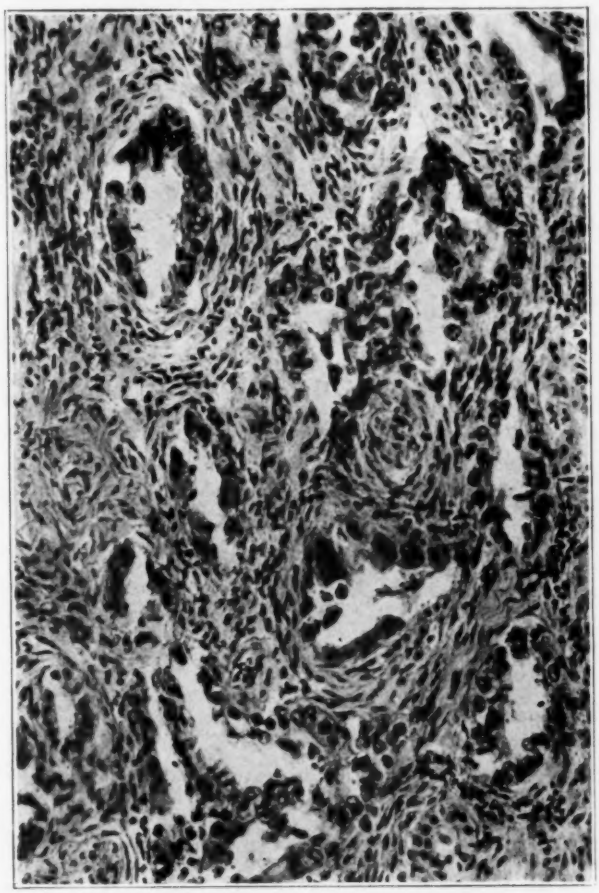

Fig. 3.—Primary adenocarcinoma of the body of the uterus. Hematoxylin and eosin stain; × 100.

knee jerk and absent ankle jerk on the left side. Abdominal reflexes were absent on the right side. The plantar responses were normal. Cutaneous sensation was unimpaired.

Metastatic lesions in the fifth and sixth dorsal vertebrae, the left hip and the left lung were seen in roentgenograms. Laboratory data were otherwise noncontributory. Lumbar puncture was not performed.

The patient became progressively weaker and died on the seventeenth day in the hospital.

*Autopsy.*—The diagnosis was: (1) status following hysterectmoy for uterine carcinoma; (2) metastases of adenocarcinoma to the liver, right kidney, adrenal glands, right lung and brain; (3) gangrenous ulceration and perforation of the rectum, with terminal peritonitis.

Gross examination of the brain revealed a solitary tumor, measuring 1.5 cm., between the cerebral hemispheres, adherent to the tip of the left frontal lobe. Microscopically the tumor was a metastatic adenocarcinoma (fig. 6). The spinal cord was normal in gross and microscopic appearance.

*Comment.*—This case, like the preceding one, illustrates that a single metastasis to the central nervous system may occur in a patient

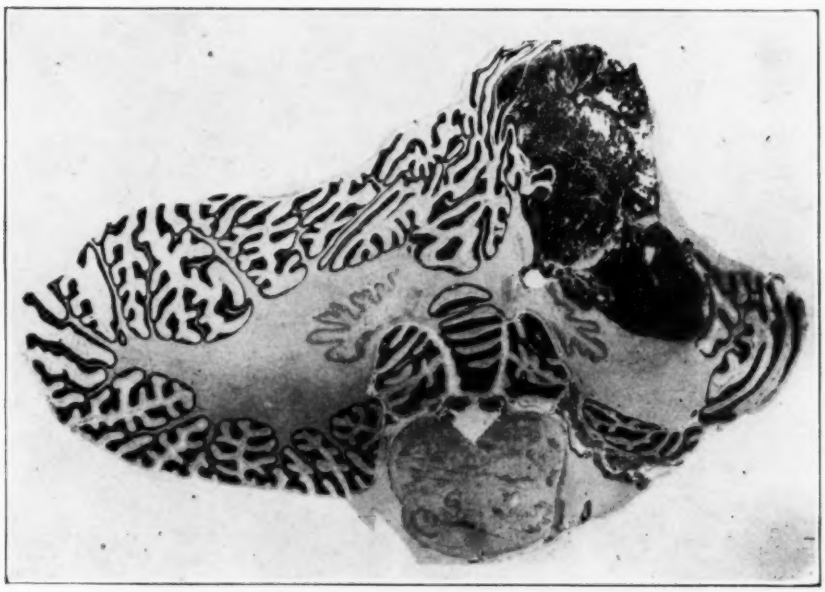

Fig. 4.—Circumscribed solitary metastatic nodule in the right cerebellar hemisphere. Cresyl violet stain; × 1.

with carcinomatosis secondary to a malignant growth in the uterine fundus.

### CASES FROM THE LITERATURE

Two cases of metastatic tumor of the brain from carcinoma of the uterus are summarized from the literature because they illustrate important points.

Hodge and Steelman[1] reported the case of a woman aged 47 who had an adenocarcinoma of the uterus removed sixteen months after the onset of abnormal vaginal bleeding. Four months before operation weakness of the right leg developed, and five months after operation the patient began to have jacksonian seizures,

1. Hodge, G. B., and Steelman, H. F.: Carcinoma of the Uterine Fundus with Metastasis to the Brain: Report of a Case, Arch. Neurol. & Psychiat. **53**:218-221 (March) 1945.

starting in the right foot. Neurologic examination revealed weakness and spasticity of the right lower extremity and hypoactive tendon reflexes on the right. There were no cranial nerve palsies or papilledema. Because the possibility of a primary cerebral tumor could not be excluded, craniotomy was performed, and a tumor, 4 cm. in diameter, located 2 cm. below the surface of the motor and sensory cortex on the left side was shelled out. The microscopic appearance of this tumor was identical with that of the uterine tumor. The patient lived for two years and at no time showed evidence of metastasis other than the one to the brain.

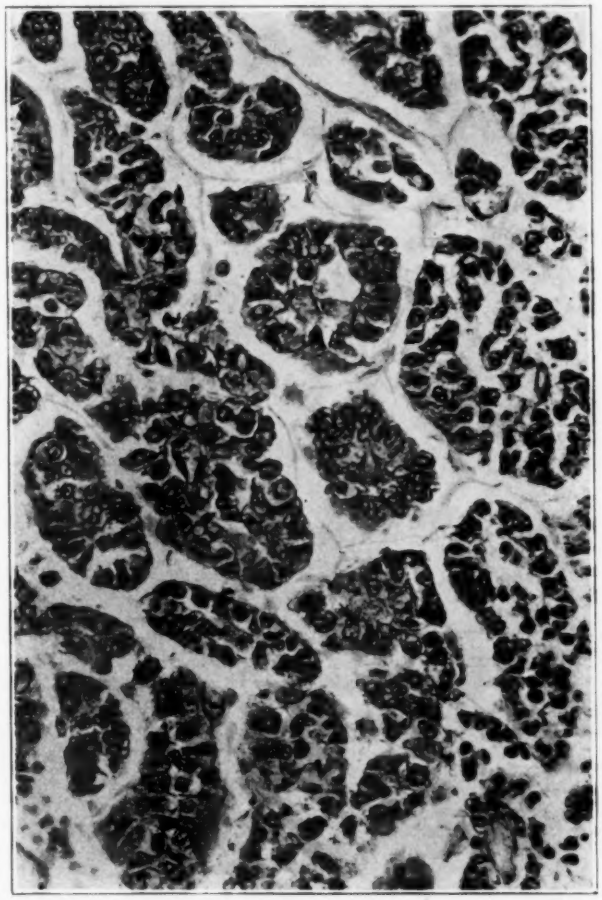

Fig. 5.—Metastatic tumor of the brain from an adenocarcinoma of the uterus. Compare this section with figure 3. Hematoxylin and eosin stain; × 100.

Mitchell and Angrist [2] reported the case of a woman aged 28 with signs and symptoms of multiple sclerosis of three years' duration. At the time of her final admission to the hospital the patient's complaints were difficulty in walking, incontinence of urine and feces and personality change. Abnormal neurologic findings were bilateral temporal pallor of the optic disks; weakness of the right side of the

2. Mitchell, N., and Angrist, A.: Massive Metastasis to the Brain from Primary Uterine Carcinoma Complicating an Advanced Case of Multiple Sclerosis, Am. J. Clin. Path. **12**:232-238 (April) 1942.

face of central origin; right hemiparesis; intention tremor; hyperactive tendon reflexes, more pronounced on the right; absence of abdominal reflexes; bilateral Babinski sign, and impairment of vibration and position sense. The cerebrospinal fluid pressure was 80 mm. of water. Two weeks later the margins of the optic disks were noted to be hazy. The patient died shortly afterward, of bronchopneumonia. Autopsy revealed, in addition to signs of extensive multiple sclerosis, a single tumor, 4.5 by 5.5 cm., in the left parietal lobe. Microscopically the tumor was an adenocarcinoma. The uterus contained an anaplastic adenocarcinoma. No metastasis other than that to the brain was encountered.

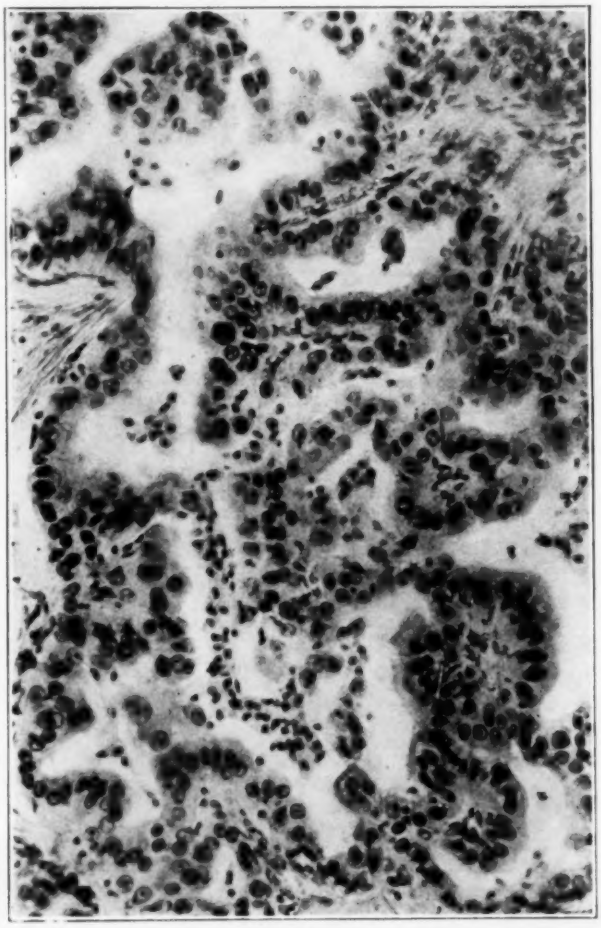

Fig. 6.—Metastatic adenocarcinoma from the brain. Hematoxylin and eosin stain; × 100.

## INCIDENCE OF METASTASES

The incidence of these metastases may be expressed in two ways: (*a*) the percentage of metastatic tumors of the central nervous system arising from carcinoma of the uterus, and (*b*) the percentage of carcinomas of the uterus metastasizing to the central nervous system. The two aspects will be considered separately.

The percentage of metastatic tumors of the central nervous system arising from carcinoma of the uterus lies between 1 and 3 per cent (table 1). Of the 128 pathologically verified metastatic tumors of the central nervous system studied at the Montefiore Hospital in the past twenty years, 16 were sarcomas, 5 hypernephromas and 107 carcinomas, 3 of which arose in the uterus. In table 2 the primary sites of these tumors are listed.

The percentage of carcinomas of the uterus metastasizing to the central nervous system is not known accurately, partly because several large surveys in the literature were based on cases which were not sub-

TABLE 1.—*Percentage of Metastatic Tumors of the Central Nervous System Arising from Uterine Carcinoma*

| Series | No. of Cases of Metastatic Carcinoma to Central Nervous System | Cases with Primary Tumor in Uterus | | |
|---|---|---|---|---|
| | | Unverified Pathologically | Verified Pathologically | Percentage |
| Neustaedter, M.: Arch. Neurol. & Psychiat. **51**: 423-425 (May) 1944 | 143 | 3 | .. | 2 |
| Montefiore Hospital | 107 | .. | 3 | 3 |
| Hare, C. C., and Schwartz, G. A.: Arch. Int. Med. **64**: 542-565 (Sept.) 1939 | 100 | .. | 1 | 1 |
| Dunlap [4] | 95 | 1 | .. | 1 |
| Elkington, J. S.: Proc. Roy. Soc. Med. **28**: 1080-1096 (June) 1935 | 72 | .. | 0 | 0 |
| Globus, J. H., and Meltzer, T.: Arch. Neurol. & Psychiat. **48**: 163-226 (Aug.) 1942 | 49 | .. | 0 | 0 |
| Meagher and Eisenhardt [10] | 44 | .. | 0 | 0 |
| Krasting [3] | 39 | .. | 4 | 10 |
| Grant [6] | 36 | .. | 0 | 0 |
| Pass, K. E.: Nervenarzt **11**: 385-400 (Aug.) 1938 | 32 | 1 | .. | 3 |
| Behrend, C. M., and Schiff, E.: Nervenarzt **11**: 57-62 (Feb.) 1938 | 20 | 1 | .. | 5 |
| German [9] | 14 | .. | 0 | 0 |
| Globus, J. H., and Selinsky, H.: Arch. Neurol. & Psychiat. **17**: 481-513 (April) 1927 | 9 | .. | 0 | 0 |

ject to a complete pathologic study. The percentages range from 0.1 to 3.4 per cent (table 3). Whether or not the percentage of uterine carcinomas metastasizing to the central nervous system is less than the percentage of carcinomas of other organs metastasizing to the central nervous system along the same channels (presumably blood borne via the lungs or the vertebral veins) will not be known until statistics from series with complete autopsies are available in larger quantity. The statistics from Krasting's [3] small series, which, oddly, contains no cases of metastasis from pulmonary carcinomas, is presented in table 4. It is the only study of the percentages of carcinomas of various organs metastasizing to the central nervous system that can be found in the literature of the past forty years.

Table 5 is an attempt to determine the index of frequency of metastasis from carcinomas of various organs to the central nervous

3. Krasting, K.: Beitrag zur Statistik und Kasuistik metastatischer Tumoren, besonders der Carcinommetastasen im Zentralnervensystem, Ztschr. f. Krebsforsch. **4**:315-379, 1906.

system. The values in the table are the ratios of the following percentages:

$$\frac{\%\text{ of carcinomas of the central nervous system metastasizing from organ X}}{\%\text{ of carcinomas primary in organ X}}$$

The percentage of carcinomas of the central nervous system metastasizing from organ X is based on the Montefiore Hospital series (table 2)

TABLE 2.—*Primary Sites of Metastatic Tumors of the Brain: Montefiore Hospital Series*

| Type | Primary Sites | No. of Cases with Full Autopsy | No. of Cases with Pathologic Study of Metastasis Only | Percentage of Total No. of Carcinomas |
|---|---|---|---|---|
| Carcinoma | Adrenal | 1 | .. | 0.9 |
| | Antrum | 1 | .. | 0.9 |
| | Breast | 41 | 6 | 44.5 |
| | Colon | 2 | .. | 1.9 |
| | Gallbladder | 1 | .. | 0.9 |
| | Liver | .. | 1 | 0.9 |
| | Lung | 37 | 4 | 38.8 |
| | Nasopharynx | 1 | .. | 0.9 |
| | Ovary | 2 | .. | 1.9 |
| | Rectum | 2 | .. | 1.9 |
| | Skin (scalp) | 1 | .. | 0.9 |
| | Sphenoidal sinus | 2 | .. | 1.9 |
| | Thyroid | 1 | .. | 0.9 |
| | Uterus | 3 | .. | 2.8 |
| | Unknown | 1 | | |
| Hypernephroma | | 5 | | |
| Sarcoma | Antrum | 2 | | |
| | Femur | 1 | | |
| | Pancreas | 1 | | |
| | Parotid | 1 | | |
| | Unknown | 2 | 2 | |
| Lymphoblastoma | Unknown | 3 | | |
| Melanosarcoma | Ear | 1 | | |
| | Foot | 1 | | |
| | Unknown | .. | 2 | |

TABLE 3.—*Percentage of Uterine Carcinomas Metastasizing to Central Nervous System*

| Series | No. of Cases of Uterine Carcinoma | No. of Cases with Metastases to Central Nervous System | Percentage | Fulll Autopsy in All Cases |
|---|---|---|---|---|
| Willimsky, W. F.: Die Metastasen des Uteruscarcinoms in entfernteren Organen, Thesis, Berlin, E. Ebering, 1904 | 1,122 | 3 | 0.3 | No |
| Krasting [3] | 116 | 4 | 3.4 | Yes |
| Glockner, cited by Offergeld [5] | 974 | 1 | 0.1 | No |
| Müller, cited by Offergeld [5] | 65 | 1 | 1.5 | No |
| Rau, W.: Ztschr. f. Krebsforsch. **18**: 141-170, 1922 | 58 | 0 | 0.0 | Yes |

and the percentage of carcinomas primary in organ X is based on a collection of 3,350 cases of carcinoma with autopsy reported by other authors (table 6). The ratios so derived are generally of the same magnitude as those derived from Krasting's statistics, shown in table 4.

Table 5 suggests that carcinoma of the breast, lung, pharynx, thyroid, sinuses and adrenal gland may metastasize more frequently to the central nervous system than carcinoma of the uterus, whereas carcinomas of the stomach, urinary bladder, pancreas and probably esophagus may metastasize less frequently.

TABLE 4.—*Percentages of Carcinomas of Various Organs Metastasizing to Central Nervous System*

(Krasting's [3] Series, All with Complete Autopsy)

| Site of Primary Carcinoma | No. of Cases | No. of Cases with Metastases to Central Nervous System | Percentage |
|---|---|---|---|
| Adrenal | 3 | 1 | 33.3 |
| Breast | 53 | 10 | 18.9 |
| Chorioepithelioma | 2 | 2 | 100.0 |
| Esophagus | 74 | 4 | 5.4 |
| Gallbladder | 37 | 2 | 5.4 |
| Maxilla (inferior) | 5 | 1 | 20.0 |
| Maxilla (superior) | 4 | 1 | 25.0 |
| Pharynx | 8 | 2 | 25.0 |
| Prostate | 18 | 4 | 22.2 |
| Rectum | 44 | 1 | 2.3 |
| Sigmoid | 20 | 1 | 5.0 |
| Thyroid | 23 | 2 | 8.7 |
| Uterus | 116 | 4 | 3.4 |
| Vagina | 2 | 1 | 50.0 |
| Vulva | 4 | 2 | 50.0 |

TABLE 5.—*Index of Frequency of Metastases from Carcinomas of Various Organs to the Central Nervous System*

| Organ | Ratio: $\frac{\text{Percentage carcinomas metastatic from organ X}}{\text{Percentage carcinomas primary in organ X}}$ | Ratio from Krasting's Series (Table 4) |
|---|---|---|
| Adrenal | 3 | 15 |
| Biliary tract | 0.2 | 3 |
| Breast | 10 | 10 |
| Esophagus | 0 | 3 |
| Intestine | 0.3 | 2 |
| Liver | 0.8 | 0 |
| Lung | 12 | 0 |
| Nasopharynx and sinuses | 6 | 13 |
| Ovary | 1 | 0 |
| Pancreas | 0 | 0 |
| Prostate | 0 | 11 |
| Skin | 1 | 0 |
| Stomach | 0 | 0 |
| Thyroid | 3 | 4 |
| Urinary bladder | 0 | 0 |
| Uterus | 0.3 | 1 |

## FREQUENCY OF SOLITARY METASTASIS TO THE CENTRAL NERVOUS SYSTEM

Metastatic tumors to the central nervous system are usually multiple. It is possible, however, that carcinomas in some organs may give rise to solitary metastasis to the central nervous system more frequently than those in other organs. The evidence, summarized in table 7, suggests that metastases from carcinomas of the uterus to the central nervous system are often solitary. In this series of 26 cases, 70 per cent had a

single metastasis to the nervous system. More statistics are needed to clarify this point. It is hoped that future statistical surveys will avoid such classifications as "carcinoma of the ovary and uterus" and "carcinoma of the genitourinary tract," which do not take into account the possibly different metastatic behavior of various tumors.

### FREQUENCY OF METASTASIS TO THE CENTRAL NERVOUS SYSTEM WITHOUT CARCINOMATOSIS

A pertinent neurosurgical consideration is whether carcinomas from certain organs may metastasize to the central nervous system in the absence of carcinomatosis. Dunlap [4] generalized: "Metastasis in general

TABLE 6.—*Site of Primary Tumor in 3,350 Cases of Carcinoma with Autopsy* *

| Organ | No. of Cases | Percentages |
|---|---|---|
| Adrenal | 1 | 0.03 |
| Biliary tract | 175 | 5.2 |
| Breast | 139 | 4.2 |
| Esophagus | 331 | 9.9 |
| External genitals | 43 | 1.3 |
| Intestine | 473 | 14.1 |
| Kidney | 33 | 1.0 |
| Larynx | 47 | 1.4 |
| Liver | 42 | 1.3 |
| Lung | 110 | 3.3 |
| Mouth, lips and pharynx | 97 | 2.9 |
| Nose and sinuses | 11 | 0.3 |
| Ovary | 65 | 1.9 |
| Pancreas | 95 | 2.8 |
| Prostate | 95 | 2.8 |
| Skin | 35 | 1.0 |
| Stomach | 1,044 | 31.2 |
| Thyroid | 10 | 0.3 |
| Tongue | 49 | 1.5 |
| Urinary bladder | 104 | 3.1 |
| Uterus | 351 | 10.5 |

* Figures represent the combined statistics of the following authors: DeVries, W. M.: The Prevalence of Cancer, in Cancer Control, Chicago, The Surgical Publishing Company of Chicago, 1927, pp. 217-246. Scholte, cited by DeVries. Bilz, cited by DeVries. Wells, H. G.: Cancer Statistics as They Appear to a Pathologist, J. A. M. A. **88**: 399-403 (Feb. 5) 1927.

is widespread throughout the body in those cases in which there is cerebral metastasis." Statistics on this matter applying to carcinoma of the uterus seem to be nonexistent. In several of the 20 cases of metastases to the central nervous system from uterine carcinoma reported by Offergeld,[5] autopsy showed absence of generalized carcinomatosis. This is true, also, of the cases reported by Hodge and Steelman and by Mitchell and Angrist and of case 1 reported here. It can be concluded,

4. Dunlap, H. F.: Metastatic Malignant Tumors of the Brain, Ann. Int. Med. **5**:1274-1288 (April) 1932.

5. Offergeld, H.: Ueber die Metastasierung des Uteruscarzinnoms in das Zentralnervensystem und die höheren Sinnesorgane, Ztschr. f. Geburtsh. u. Gynäk. **63**:1-36, 1908-1909.

therefore, that carcinomas of the uterus metastasize to the central nervous system not infrequently in the absence of generalized metastatic disease. The role played by the vertebral veins in such metastasis is not clear.

### THERAPY

The usefulness of neurosurgery in cases of metastatic tumors of the brain has been discussed in the literature. Grant [6] stated that in cases of metastatic brain tumor ". . . neither radical nor palliative surgery is of any permanent avail." His conclusion was based on a series of 47 cases of metastatic tumors of the central nervous system, in 25 of which operation was performed and in 22 of which it was not. The average length of life from the time of hospitalization to death was less than four months regardless of whether or not operation was performed. Grant's observations were in accord with those of Tooth.[7] Oldberg,[8] however, reported 3 cases of metastatic tumor of the central nervous system in which there was definite prolongation of life after neurosurgical intervention, just as in Hodge and Steelman's case. He sug-

TABLE 7.—*Percentage of Solitary Metastatic Tumors of the Central Nervous System from Uterine Carcinoma*

| Source | No. of Cases of Uterine Metastases to Central Nervous System | No. of Cases with Metastases to Central Nervous System | | |
|---|---|---|---|---|
| | | One Metastasis | Two Metastases | Multiple Metastases |
| Offergeld [5] | 14 | 9 | 2 | 3 |
| Krasting [3] | 4 | 2 | 1 | 1 |
| Montefiore Hospital | 3 | 3 | 0 | 0 |
| Willimsky, W. F.: Die Matastasen des Uteruscarcinoms in entfernteren Organen, Thesis, Berlin, E. Ebering, 1904 | 3 | 2 | 0 | 1 |
| Hodge and Steelman [1] | 1 | 1 | 0 | 0 |
| Mitchell and Angrist [2] | 1 | 1 | 0 | 0 |
| Total number of cases | 26 | 18 | 3 | 5 |
| Percentage | 100% | 70% | 11% | 19% |

gested that before operating for a suspected metastatic tumor of the brain one should check for clinical evidence of multiplicity of metastases to the central nervous system and for clinical evidence of metastases elsewhere, and prognosticate as to the course or recurrence of the primary focus. German [9] stated:

> The conclusion is drawn that operation is definitely indicated in patients with metastatic carcinoma of the brain if the metastasis is apparently solitary.

6. Grant, F. C.: Intracranial Malignant Metastases: Their Frequency and Value of Surgery in Their Treatment, Ann. Surg. **84**:635-646, (Nov.) 1926.

7. Tooth, H. T.: The Treatment of Tumors of the Brain and Indications for an Operation, Tr. Internat. Cong. Med., London, sect. VII, Surg., 1913, pp. 203-299.

8. Oldberg, E.: Surgical Consideration of Carcinomatous Metastases to the Brain, J. A. M. A. **101**:1458-1461 (Nov. 4) 1933.

9. German, W. J.: Carcinomatous Metastases to the Brain, Ann. Surg. **108**: 980-991 (Dec.) 1938.

Oldberg [8] and Meagher and Eisenhardt [10] reported a case of suspected metastatic brain tumor which at operation was found to be a primary brain tumor. A similar experience was encountered recently at this hospital in the case of a woman aged 54 with signs and symptoms of an expanding intracranial lesion. Ten years previously the patient had received roentgen therapy for a uterine carcinoma. Physical examination failed to reveal any sign of recurrence or metastasis of the cancer except for the probable existence of a cerebral metastasis. Because of the woman's poor physical condition and because the accepted diagnosis was metastatic tumor of the brain, craniotomy was not performed. The patient died, and at autopsy her death was attributed to the cerebral tumor—a large glioblastoma multiforme. There was no pathologic evidence of recurrence or metastasis of the uterine carcinoma to any part of the body.

Neurosurgical intervention is contraindicated in most cases of metastatic tumor of the brain secondary to the uterine carcinoma because of the frequent accompaniment of carcinomatosis. But when, as in case 1, there is no evidence of this complication and when signs suggest a solitary brain tumor, neurosurgical intervention may prolong life.

SUMMARY

Metastases from carcinoma of the uterus probably account for 1 to 3 per cent of all carcinomas of the central nervous system.

The percentage of uterine carcinomas metastasizing to the central nervous system varies from 0.1 to 3.4 per cent, according to different sources.

Carcinoma of the breast, lung, pharynx, sinuses, thyroid and adrenal gland may metastasize more frequently to the central nervous system than carcinoma of the uterus, whereas carcinoma of the stomach, urinary bladder, pancreas and esophagus may metastasize less frequently.

There is evidence that metastases to the central nervous system from uterine carcinoma are often solitary.

Uterine carcinoma may metastasize to the central nervous system in the absence of carcinomatosis.

In cases in which metastasis to the central nervous system from a carcinoma of the uterus is suspected, neurosurgical exploration is indicated only if there is no evidence of multiple metastases to the brain or spinal cord and no evidence of carcinomatosis.

11 East Thirty-Sixth Street.

Montefiore Hospital for Chronic Diseases.

10. Meagher, R., and Eisenhardt, L.: Intracranial Carcinomatous Metastases, with Note on Relation of Carcinoma and Tubercle, Ann. Surg. **93**:132-140 (Jan.) 1931

# SCHISTOSOMIASIS OF THE BRAIN DUE TO SCHISTOSOMA JAPONICUM

## Report of a Case

CAPTAIN CHARLES WESLEY WATSON

LIEUTENANT COLONEL FRANCIS MURPHEY
AND
MAJOR SAMUEL C. LITTLE
MEDICAL CORPS, ARMY OF THE UNITED STATES

THE DEPOSITION of ova in the central nervous system is a rare complication of the infection of man by the trematode Schistosoma japonicum. The demonstration of these ova in the cerebral tissue has been reported four times in the available literature,[1] and a fifth report is to be published.[2] Two reports originate in the Philippine literature and one in the British literature. Vitug, Cruz and Bautista [1a] reported 2 cases of schistosomiasis involving the brain, 1 of which was presented with histologic evidence of ova-infected cerebral tissue. A favorable response to antimony was accepted as evidence for the diagnosis in the second case. These authors found two reports in the Philippine literature referring to schistosomiasis of the brain. Nieva [3] described the case of a patient from Samar who experienced epilepsy, headaches and sensory changes. The ova of S. japonicum were found in the feces. The probable diagnosis of cerebral schistosomiasis was based on inference. Improvement followed injections of emetine hydrochloride and antimony and potassium tartrate U. S. P. Greenfield and Pritchard [1c] reported 2 cases of schistosomiasis of the brain in which the ova were

From the Section of Neurology and Neurosurgery, O'Reilly General Hospital, Springfield, Mo.

1. (*a*) Vitug, W.; Cruz, J. R., and Bautista, L. D.: Schistosomiasis Involving the Brain: Two Case Reports, J. Phillippine Islands M. A. **21**:291-298 (June) 1941. (*b*) Africa, C. M., and Cruz, J. Z.: Eggs of Schistosoma Japonicum in the Human Heart, in Volumen Jubilare pro Sadao Yoshida, Osaka, Japan, 1939, vol. 2, pp. 113-117; cited by Vitug, Cruz and Bautista.[1a] (*c*) Greenfield, J. G., and Pritchard, B.: Cerebral Infection with Schistosoma Japonicum, Brain **60**:361-372 (Sept.) 1937. (*d*) Tfunada, T., and Shimamura, S., cited by Greenfield and Pritchard.[1c]

2. Maltby, G. L., and Schmidt, J. R.: Schistosomiasis of the Cerebrum Simulating Brain Tumor, to be published.

3. Nieva, D. E.: Epileptiform Convulsions Probably Due to Schistosomiasis, Bull. San Juán de Dios Hosp., 1935, vol. 9, no. 7; cited by Vitug, Cruz and Bautista.[1a]

demonstrated histologically in the cerebral tissue of the left parietal and occipital regions. Tfunada and Shimamura,[1d] in 1906, reported a case of cerebral involvement by S. japonicum with symptoms of convulsions, aphasia and hemiplegia. Autopsy revealed abnormal masses in the parietal lobe, the internal capsule and the optic thalamus on the left side. Histologic examination revealed ova of S. japonicum. Tillman,[4] reporting experiences with soldiers on Leyte, recently described 7 cases of schistosomiasis in which there were symptoms of involvement of the central nervous system. Confusion, aphasia and hyperreflexia were noted. All the patients recovered. The diagnosis was made by inference. A patient with visceral schistosomiasis due to S. japonicum who exhibited convulsions, asphasia and evidence of increased intracranial pressure was subjected to craniotomy at England General Hospital. A biopsy of the mass removed from the left parietal region contained ova of S. japonicum.[2] A second patient with schistosomiasis due to S. japonicum observed at the same hospital had jacksonian convulsions and aphasia. A "mass of probable parasitic etiology" was detected in the left parietal lobe, in the postcentral region, but was not removed.[5] Africa and Cruz,[1b] in a report of the discovery of ova of S. japonicum in the human myocardium, mentioned that these ova were also observed in the brain. Clinical data were not given. Spiridon[6] reported an outbreak of schistosomiasis due to S. japonicum among British sailors who had bathed in the Yangtze River; 3 men infected simultaneously exhibited well defined neurologic signs and symptoms, which improved notably after treatment with antimony compounds. Hoff and Shaby[7] reported a case in which paraplegia and mental confusion were exhibited and air encephalograms revealed a mass in the lateral wall of the right ventricle. S. japonicum was observed in the stools. In the authoritative monograph on schistosomiasis by Faust and Meleney[8] it is stated that symptoms of involvement of the central nervous system, such as jacksonian epilepsy, may occur. Edgar[9] reported a case with convulsions and symptoms similar to those described by Greenfield and Pritchard.[1c]

4. Tillman, A. J. B.: Cerebral Manifestations of Schistosomiasis Japonica, abstracted, Bull. U. S. Army M. Dept. **4**:492 (Nov.) 1945.

5. Chasnoff, J.: Personal communication to the authors.

6. Spiridon, J. T.: Schistosomiasis Japonica: An Account of an Outbreak, J. Trop. Med. **39**:161-164 (July 15) 1936.

7. Hoff, H., and Shaby, J. A.: Nervous and Mental Manifestations of Bilharziasis and Their Treatment, Tr. Roy. Soc. Trop. Med. & Hyg. **33**:107-111 (June) 1939.

8. Faust, E. C., and Meleney, E. H.: Studies on Schistosoma Japonica, Monograph Series no. 3, Baltimore, American Journal of Hygiene, 1924.

9. Edgar, W. H., cited by Chalgren, W. S., and Baker, A. B.: Tropical Diseases: Involvement of the Nervous System, Arch. Path. **41**:66-117 (Jan.) 1946.

A tumor mass containing ova of S. japonicum was removed "from beneath the parietal bone."

Involvement of the central nervous system by the ova of related trematodes has been described.[10] Müller and Stender [10b] described a verified case of infection of the spinal cord by the ova of Schistosoma mansoni. Chung [10d] reported a case of bilharziasis with neurologic signs. Spiridon [6] stated that Mann, of the United States Naval Medical Service, recorded an outbreak of bilharziasis in which jacksonian epilepsy, hemiplegia and aberrations of personality resembling schizophrenia were mentioned. Khaw, of Peiping, China, in a communication to Spiridon,[6] described a case of bilharziasis with neurologic signs. In few cases can autopsy be performed. Ferguson [10e] reported that he had observed the ova of Schistosoma haematobium in the brain and the spinal cord.

## REPORT OF CASE

*History.*—On Dec. 12, 1944, one and one-half weeks after the patient, an infantryman, landed on Leyte, Philippines, he swam in a river which was later condemned for swimming, laundry and drinking purposes. One and one-half weeks later he noted the onset of anorexia, the first symptom. Two weeks after exposure he experienced intermittent coughing and moderately severe, sharp pain in the right upper abdominal quadrant, which occurred in the morning and the evening and was accentuated after the ingestion of food. Three days after onset of the abdominal pain, or seventeen days after exposure, the patient had a regular intermittent fever, with diarrhea and vomiting. The temperature curve rose and fell over a period of one hour, at approximately 8: 30 in the morning, reaching a maximum of 101 F.; and then returning to normal, it showed a gradual elevation during the early afternoon, reaching a maximum of 103 F. at approximately 8:30 p. m., and returning to normal one-half hour later. This type of fever was present daily without alteration or cessation until March 28, 1945, after which for six days the patient experienced a continuous fever of 102 F. throughout the day and night. On April 2 the patient was given eleven tablets of sulfadiazine and four tablets of acetylsalicylic acid at one time. There was cessation of the fever, with return to normal. There has been no fever since that time. The diarrhea, which began on December 29, was intermittent, without gross blood or mucus, and continued until the patient returned to the United States. The vomiting, which began December 29, was sudden in onset, violent but nonprojectile, and occurred as often as thirty times a day for a period of fifteen days, the vomitus consisting of green, bitter-tasting material and containing no gross blood or fecal contamination. One hundred and nine days after exposure the patient was hospitalized because of

10. (*a*) Spiridon.[6] (*b*) Müller, H. H., and Stender, A.: Bilharziasis of the Spinal Cord Presenting the Picture of Myelitis Dorsolumbalis Transversa Completa, Arch. f. Schiffs- u. Tropen-Hyg. **34**:537-538 (Oct.) 1930. (*c*) Yamigawa, K.: The Etiology of Jacksonian Epilepsy, Virchows Arch. f. path. Anat. **119**:447-460, 1890. (*d*) Chung, H. L.: Certain Surgical Complications of Schistosomiasis Japonica, China M. J. **47**:1171-1180 (Nov.-Dec.) 1933; cited by Vitug, Cruz and Bautista.[1a] (*e*) Ferguson, A. R., cited by Chalgren, W. S., and Baker, A. B.: Tropical Diseases: Involvement of the Nervous System, Arch. Path. **41**:66-117 (Jan.) 1946.

the fever, diarrhea and abdominal cramps. Examination of the stool on April 2 and April 6 revealed the presence of ova of S. japonicum. Beginning on April 8, ten intramuscular injections of emetine hydrochloride, containing 1 grain (0.065 Gm.) each, were administered. There was no other treatment with antimony preparations prior to admission to O'Reilly General Hospital.

Between April 6 and June 24, 1945, laboratory procedures were carried out as follows: Hematologic examination revealed 12,000 to 22,000 leukocytes per cubic millimeter, with persistent eosinophilia, the latter reaching 32 to 74 per cent. The hemoglobin measured 8.6 to 15 Gm. (a normal content followed the transfusion of 500 cc. of whole blood). Examination of the cerebrospinal fluid on May 24 revealed 3 lymphocytes per cubic millimeter, a normal colloidal gold curve, a negative Wassermann reaction and 30 mg. of protein per hundred cubic centimeters. Repeated examinations of the stool and urine showed nothing abnormal except for occult blood in the stool on two occasions. The blood sugar measured 78 mg. per hundred cubic centimeters.

In the same period, during which the patient passed through three hospital installations, he became progressively more emaciated and experienced daily cramping pain in the right upper abdominal quadrant, tenderness on abdominal pressure and recurrent seizures, which will be described later. Physical and neurologic examinations performed at each installation revealed a similar picture. Significant findings included emaciation; palpable liver, spleen and kidneys; abdominal tenderness, and distention of the superficial veins of the lower part of the abdomen.

The patient experienced ten seizures prior to his admission to O'Reilly General Hospital, on June 24. In general, the seizures were of grand mal and psychomotor equivalent types. The first seizure, which occurred on the one hundred and fifty-sixth day following exposure, which presumably was Dec. 12, 1944, was initiated by radiating headaches of great violence in the left prefrontal lesion; loss of consciousness followed, and there were postictal confusion and an amnesic type of aphasia. A second seizure was similar, but there was a jacksonian "march," beginning in the right leg and progressing to generalized clonic movement, without loss of consciousness. The patient had delayed mixed aphasia, amnesia for the episode, postictal headache on the left side, abdominal pain and vomiting. The fifth seizure was noteworthy for uncontrollable weeping and laughing without appropriate emotional disturbance. Urinary incontinence occurred on one occasion. Between June 15 and June 24 there were five seizures, of varying severity, but all were characterized by similar symptoms.

Phenobarbital was given irregularly after the seizures and in variable doses. Diphenylhydantoin sodium (0.2 Gm. daily) was given from the one hundred and sixty-seventh day following exposure to the time of his admission to the general hospital.

*Examination.*—On arrival at the general hospital, on the one hundred and ninety-fourth day following exposure, the patient appeared undernourished, extremely emaciated but alert, pleasant and not acutely ill. The family history and the past personal history revealed nothing of significance. Routine physical examination showed "shotty" enlargement of the inguinal and epitrochlear lymph nodes. The abdominal viscera could not be palpated satisfactorily because of increased tension of the abdominal muscles, but it was determined by percussion that the edge of the liver extended 4 cm. below the right costal margin. Superficial veins over the lower part of the abdomen were moderately distended and collapsed

when the patient lay in the horizontal position, the blood appearing to drain downward.

Neurologic examination on his admission, including studies of gnosis, praxis and phasia, showed nothing abnormal except for a slight "rolling" gait (superficially resembling the cerebellar type) and slight confusion of laterality.

Between June 24 and July 5, laboratory procedures were carried out as follows: Hematologic examination revealed 5,750 leukocytes per cubic millimeter, with a normal differential count; 3,870,000 erythrocytes, 85 to 95 per cent hemoglobin; a hematocrit reading of 39 per cent, and a sedimenation rate of 19 mm. in one hour (diagonal curve, Crile method). The cerebrospinal fluid on June 28 showed a pressure of 130 mm. of fluid, normal dynamics, 1 lymphocyte per cubic millimeter, a total protein content of 100 mg. and a glucose content of 56.8 mg. per hundred cubic centimeters, a negative Wassermann reaction, a sterile culture and a colloidal gold curve of 5542100000. No eosinophils or ova were found in the centrifuged

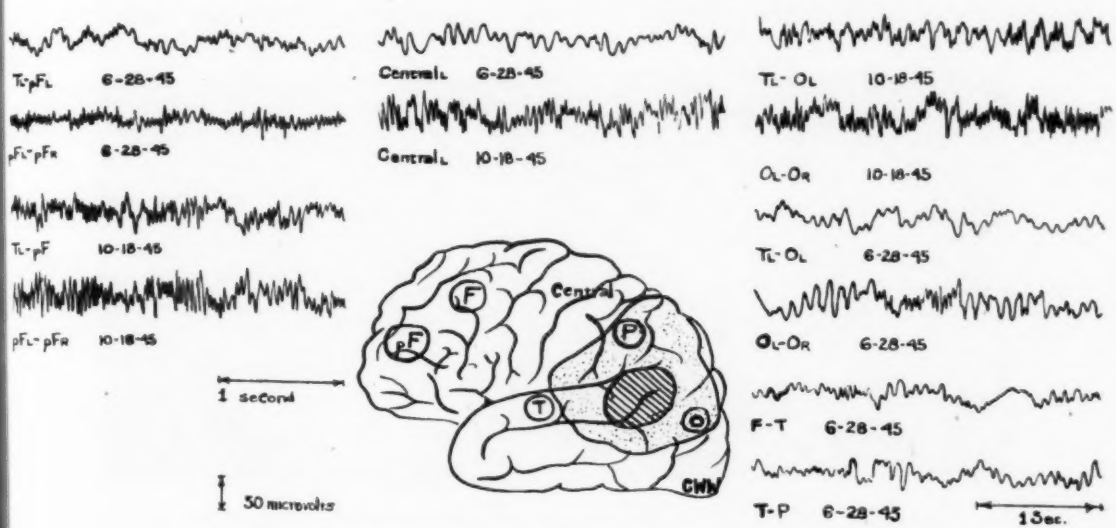


Fig. 1.—Composite chart showing electroencephalographic tracings in a case of schistosomiasis of the brain. All tracings were recorded under standard conditions. Technical data are indicated below the tracings. In this figure, *pF* means prefrontal; *F*, frontal; *central*, the rolandic fissure; *P*, parietal; *O*, occipital; *T*, temporal, and *r* and *l*, right and left. The appropriate date is recorded immediately beneath each tracing. The area of cross hatching indicates the preoperative localization of the lesion by electroencephalographic recording. The shaded area shows the area of "neighborhood signs," as indicated electroencephalographically. The slow activity with "phase reversal" which permitted preoperative localization is illustrated by the four tracings in the lower right corner of the figure. The two tracings in the upper right corner are to be compared with the two tracings immediately beneath. The progression of "epileptogenic activity" is notable. The rest of the tracings illustrate the progression of "epileptogenic activity" as recorded from the same areas on various occasions.

specimen of the cerebrospinal fluid. Urinalysis, biopsy of muscle and roentgenographic examination of the chest and the cervical portion of the spine revealed nothing abnormal. Repeated examinations of the stool, including concentration and egg-hatching technics for ova of trematodes, consistently revealed no parasites. The serum cephalin-cholesterol flocculation test gave a 1 plus reaction; the total serum protein measured 5.4 Gm., with 2.9 Gm. of albumin and 2.5 Gm. of globulin

(ratio of albumin to globulin, 1 : 1), and the icteric index was 4. Roentgenograms of the skull revealed a calcified pineal gland, which was displaced 1.2 cm. to the right and posteriorly.

The preoperative electroencephalogram (fig. 1) was abnormal, with localization of abnormally slow activity showing "phase reversal" in the region of the posterior third of the superior temporal gyrus, including the superior portion of the angular gyrus and the inferior portion of the supramarginal gyrus. There was definite generalized "epileptogenic activity." Electroencephalographic abnormalities, with graphic illustration of the progressive enhancement of epileptogenic activity, are shown in figure 1.

*Preoperative Course.*—From the time of admission, on June 24, to July 27, the patient experienced only five disorders of consciousness. Thereafter, despite frequent upward revisions of medication and the inclusion of phenobarbital, until he eventually was receiving 0.7 Gm. of diphenylhydantoin sodium and 0.3 Gm. of phenobarbital daily, he continued to have as many as six seizures daily, with

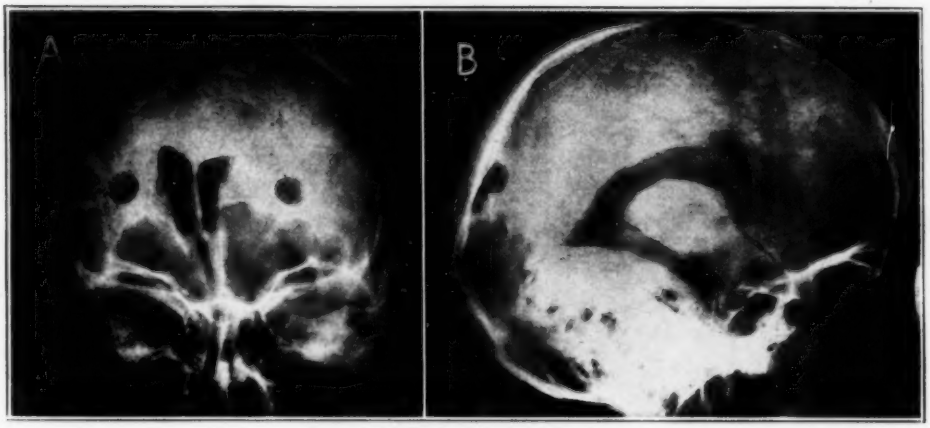


Fig. 2.—*A*, ventriculogram showing shift of the ventricular system to the right as a result of a space-occupying lesion of the left temporal region. *B*, ventriculogram showing displacement of the temporal horn of the left lateral ventricle and intracranial calcification. The excised granuloma contained calcium.

variable symptoms. Sometimes there was a prodrome of alexia associated with an amnesic type of aphasia which lasted five minutes and was followed by severe headache in the left temporal area. Some seizures began with micropsia and were followed by severe headaches in the left temporal regions. Some seizures began with micropsia and were followed by clonic movements of the right arm, spreading to the right leg and finally over the entire body. In this type, there was no loss of consciousness, tongue biting or incontinence of urine or feces, but immediately after the seizure uncontrollable copious weeping occurred. One attack was followed by a right homonymous field defect with macular sparing. A detailed examination twelve hours later revealed no evidence of visual impairment. Visual agnosia was absent.

*Ventriculographic Study and Operation.*—A pneumoencephalogram was attempted on July 2, but ventricular filling did not occur. On July 5 a ventriculographic study showed a large expanding lesion in the left parietotemporal region. Opacity, suggestive of abnormal intracranial calicification, was present in the

region of the posterior portion of the left temporal horn. One hour after the ventriculogram was taken an exploratory parietotemporal craniotomy was performed. The dura, when exposed, was seen to be tense and could be opened only after a spinal puncture had been made and the intracranial pressure reduced. An area of discoloration and induration, with multiple irregular, tiny white nodules, was observed in the posterior third of the superior temporal gyrus. At one point it invaded the dura. This area measured 2 cm. in diameter on the surface of the cortex and seemed to extend subcortically into the angular and supramarginal gyri. The entire mass was estimated to be 5 or 6 cm. in diameter. An incision was made into the mass, and the tissue had the gross appearance of a glioblastoma multiforme. A biopsy specimen was obtained, and frozen sections were made. A definite diagnosis could not be made from these sections, but the appearance was suggestive of an invasive glioma. Since complete resection of the mass would have resulted in a serious speech defect, it was not done. A large subtemporal decompression was made and the operation terminated.

*Biopsy.*—Examination of permanent sections (hemotoxylin and eosin stain) revealed numerous focal lesions, some near and some relatively distant from blood vessels and capillaries. The typical lesion consisted of a central area of necrosis with a concentric ring of packed leukocytes, predominantly eosinophils (fig. 3). There was extensive glial proliferation but no evidence of neoplasia. Within or near the center of many of the lesions there were doubly refractile, light brown paraboloid structures, measuring approximately 60 by 40 microns with polar flattening and a single rudimentary "hook." No foreign body giant cells were observed.

*Treatment.*—On July 8 a course of treatments with fuadin was begun. Fuadin contains 13.6 per cent trivalent antimony and is supplied in ampules containing a 6.4 per cent solution of the drug (approximately 0.06 mg. of fuadin in 1 cc. of solution). The fuadin solution is injected slowly into the muscle. The first three doses, of 1.5, 3.5 and 5 cc., were given on successive days. On the fifth day, and on subsequent alternate days, 5 cc. was given, until a total of sixteen doses had been administered (75 cc. of solution, containing 0.653 Gm. of antimony). The hemogram was determined every two days, and a complete urinalysis was done at the same time. Prior to the beginning of the therapy, and periodically during the course, an electrocardiogram was taken, the serum cephalin-cholesterol flocculation test was done and the icteric index was determined. There was no evidence of renal, hepatic or myocardial dysfunction during the period of therapy. Since the seventh postoperative day, the decompression has remained soft and pulsating.

Because of the failure to control the seizures with relatively large amounts of diphenylhydantoin and phenobarbital, and because there persisted a definite focus of cerebral damage, as evidenced by repeated electroencephalograms, a second craniotomy was performed on November 5. On exposure, the dura was observed to be quite soft, and there was no evidence of increased intracranial pressure. The dura was then opened, and the lesion which previously had been present was observed to have disappeared and to have been replaced by an area of scar tissue 1.5 cm. in diameter. Numerous white, hard lesions, 1 mm. in diameter were observed over the entire field. A ventricular needle inserted toward the posterior portion of the temporal horn entered the ventricle at a depth of 2 cm., indicating that the ventricle, which had formerly been compressed, was now greatly dilated. Further exploration with a ventricular needle revealed considerable subcortical scar

tissue for a distance of approximately 5 cm. posterior to the cortical lesion. It was immediately apparent that all the scar tissue could not be removed without producing a serious speech defect, but it was thought worth while to remove the

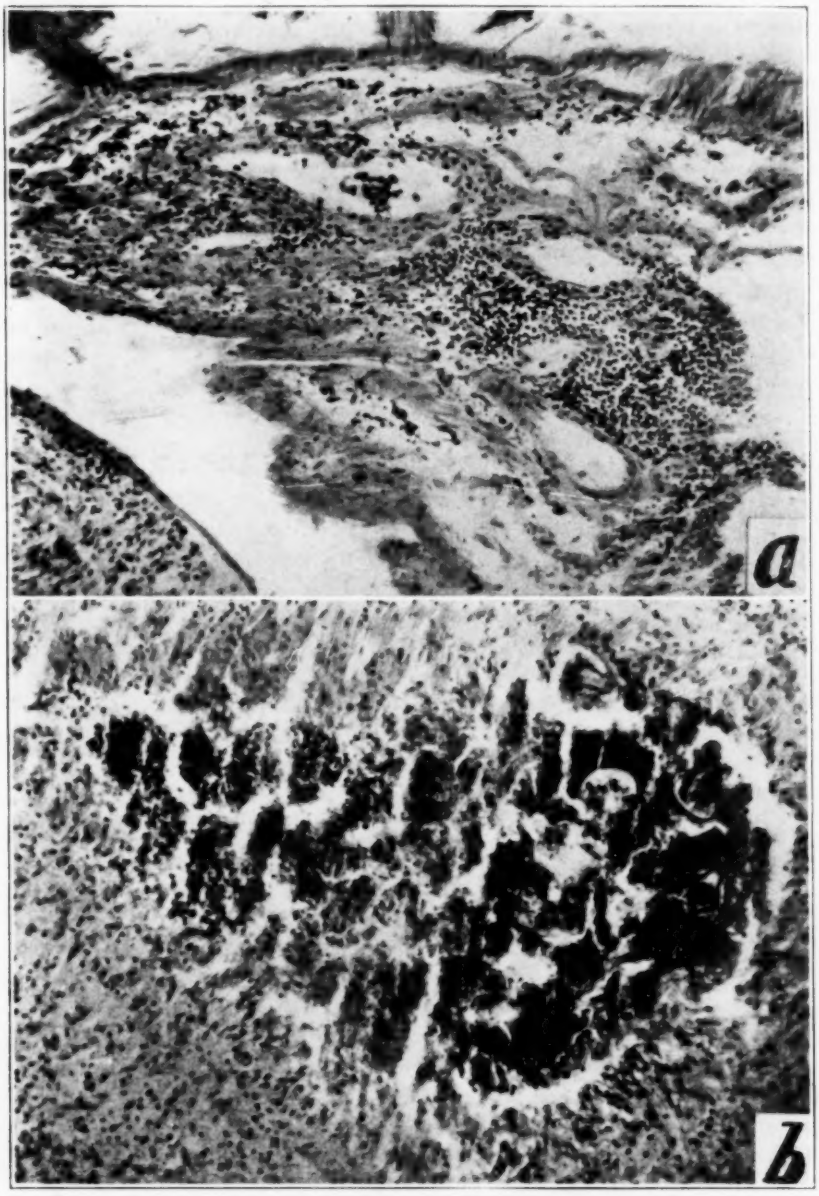


Figure 3, *A* and *B*.

superficial scar tissue which had replaced the granuloma visible at the first operation. The specimen measured approximately 1.5 by 1 by 0.5 cm. The patient had no untoward effect from the operation.

Attempts to hatch miracidia from the tissue obtained at biopsy were unsuccessful, but stained sections (hematoxylin and eosin) showed large numbers of ova of S. japonicum.

At the time of writing, it has been only four weeks since the operation, and it is obviously too early to justify our reaching any conclusions concerning the benefit of this procedure. However, it should be stated that the patient's general condition is much improved. Administration of phenobarbital has been discontinued, but in spite of this the seizures are less frequent and less severe.

## COMMENT

The route of infection of the brain by the ova of S. japonicum remains obscure. The rarity of this complication is commonly explained by the existence of the vascular barriers of the lung and liver. Ordi-

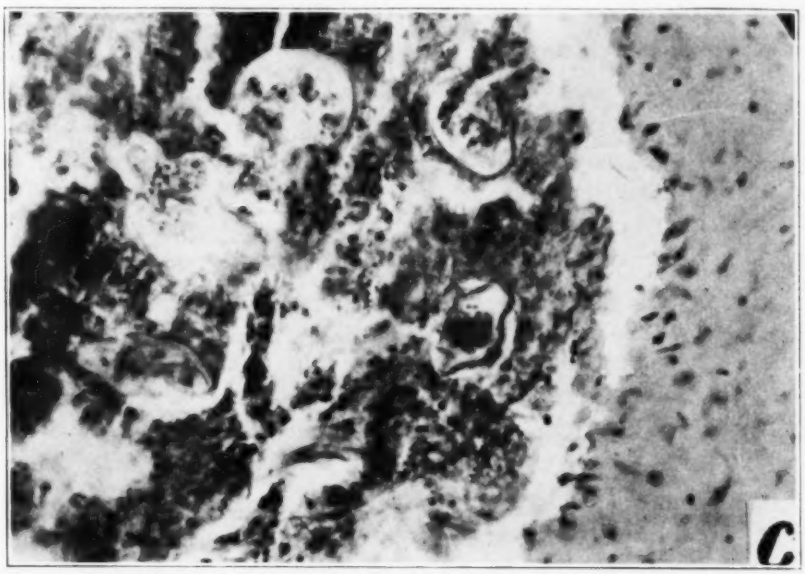


Fig. 3.—Photomicrographs showing (*a*) perivascular infiltration with round cells and eosinophils (× 140), (*b*) the typical lesion or "pseudotubercle," with gliosis, necrosis, packed eosinophils and distorted ova of Schistosoma japonicum (× 140) and (*c*) six distorted ova of S. japonicum embedded in packed, damaged eosinophils. (× 330). The "hook" is visible on the ovum in the upper right corner of this photograph.

narily, the cercariae of the trematode infect man by penetrating the skin, after which, they travel to the liver by way of the blood and lymph channels. The cercariae develop into adults, which migrate to the venules of the small intestine, where ova are deposited. By passive penetration, the ova enter the lumen of the intestine and are excreted. The life cycle is completed by hatching of the ova in water, with the liberation of ciliated miracidia, which infect certain species of snail, the distribution of which determines the distribution of the disease. After

the intramolluscan phase of multiplication and development, the resultant cercariae emerge and swim about in search of a human host. Penetration of the skin begins the intramammalian phase of the cycle. Even assuming the presence of a cardiac anomaly which would allow the passage of the ova from the venous to the arterial circulation without the impediment of the pulmonary capillary bed, there is still the barrier of the hepatic portal system. Greenfield and Pritchard [1c] noted the tendency of the ova to localize in the left cerebral hemisphere. This observation is confirmed by a review of the literature. They suggested that the adult worms lie in one of the cerebral venous sinuses, probably the lateral sinus, and migrate up the posterior anastomotic vein for the purpose of egg laying. There is yet no proof for such a hypothesis. Without the benefit of scientific explanation, the ova occasionally, nevertheless, arrive in the cerebral tissue. Faust and Meleney [8] offered no solution for the problem.

The pathologic basis for the symptoms presented by this patient lay in the lesions produced by the presence of the ova. There was an inflammatory response, characterized mainly by necrosis and the presence of large numbers of eosinophils. Calcification was evident in both gross and microscopic specimens and may have been the cause of the cerebral irritation, which became progressively more pronounced, as evidenced by the electroencephalogram and the increased difficulty in controlling the seizures (figs. 1 and 2). The juxtaposition of numerous lesions may produce the signs and symptoms of cerebral tumor, as in this case. The electroencephalographic evidence of generalized epileptogenic activity in the case in point implied wide distribution of the lesions.

The diameter of the tumor at the time of operation was approximately 5 cm. This estimate is based on the observations on the cortical surface at operation and the degree of distortion of the ventricular system. Headache was relieved immediately after operative decompression.

Language dysfunction of the receptive type, with a premonitory marked fatigue phenomenon, was present at all times and became more pronounced. The idea content of written and spoken language was appreciated to a moderately impaired degree for approximately five minutes of narrative speech. The patient was then incapable of repeating the idea content. He said, "After five minutes of listening, I can hear the individual words and the sentences and understand them, but I can't get the idea they want to put over at all."

The patient was placed under treatment with a standard course of fuadin immediately after operation and confirmation of the preoperative diagnosis. Since there was no recurrence of the headaches of the type experienced prior to operation, it may be inferred that there was some

reduction of the tumor mass due to fuadin therapy, possibly on the basis of the reduction of inflammation around the ova.

Treatment of the seizures was by use of diphenylhydantoin sodium and phenobarbital. It is of interest that the phenomenon of weeping persisted after the disappearance of micropsia and episodic dysphasia, usually in the absence of overt motor movements. This improvement was of transient character, since the seizures became progressively worse.

There is little case material to serve as a standard for prognosis. Greenfield and Pritchard [1c] stated:

> The prognosis with regard to survival and cessation of convulsive seizures is good when operative removal of the tumour is followed by a course of antimony therapy.

Of the 2 patients at England General Hospital,[2] the one who was operated on was discharged with "very slight weakness of facial muscles and occasional slurring of speech." The other patient, who was subjected merely to probing, continued to show some aphasia. Convulsions were controlled with diphenylhydantoin sodium. Both patients received fuadin therapy after operation. Seven patients reported on by Tillman [4] recovered. Some showed residual symptoms three months after exposure. Of the 2 patients with cerebral schistosomiasis reported by Vitug, Cruz and Bautista,[1a] 1 died in a convulsive attack and the other, after two months of convalescence, recovered from hemiparesis and was discharged as "strong and walking." Spiridon [6] reported on 12 patients with schistosomiasis, of whom 3 showed neurologic signs. A patient who had shown clouding of the sensorium, paresis of the arms and incontinence was given intravenous injections of sodium antimonyl tartrate and had no symptoms at the end of four weeks. A second patient, with coma, spastic quadriplegia and attacks of screaming at various times, who received similar treatment, was allowed to return home after seventeen weeks of convalescence. He had residual spastic hemiparesis. A third patient had flaccid hemiplegia, which showed improvement apparently prior to, as well as after, injections of fuadin.

Vitug, Cruz and Bautista [1a] described lesions in the choroid plexus, as well as in the parenchyma. The pia was thickened. There were fibrosis and thickening of the vessel walls with "pseudotubercles," including giant cells. Gliosis was present. The pathologic picture decribed by Greenfield and Pritchard [1c] was similar in most respects to that described in the present report. A much smaller proportion of eosinophils was observed in the lesions of their cases, however.

Faust,[11] paraphrasing Gonzales Martinez, merely stated that the egg has an "irritative action."

11. Faust, E. C.: Studies on Schistosomiasis Mansoni in Puerto Rico: I. The History of Schistosomiasis in Puerto Rico, Puerto Rico J. Pub. Health & Trop. Med. **9**:154-161 (Dec.) 1933.

The earliest symptom of cerebral involvement by the ova is usually focal epileptic seizures,[12] and the left hemisphere is most frequently involved.[12]

SUMMARY

This report deals with a case of cerebral schistosomiasis, in which the ova were demonstrated in the cerebral tissue.

There was a definite history of exposure in water, later condemned for bathing, in a region in which the disease is endemic. The onset was typical, with vague constitutional symptoms, gastrointestinal disturbance, fever and eosinophilia. Ova of S. japonicum were found in the stool. Convulsive seizures and paroxysmal disturbances of consciousness developed. There were definite electroencephalographic changes indicative of a localized intracranial space-occupying lesion and of epilepsy. A ventriculogram confirmed the presence of a space-occupying lesion, and a granuloma in the predicted location was visualized at operation. Biopsy of specimens obtained on two separate occasions revealed ova of S. japonicum. The patient's clinical course and treatment are described.

River Cottage, Forest Street, Sherborn, Mass.
899 Madison Avenue, Memphis 3, Tenn.
2167 Highland Avenue, Birmingham 5, Ala.

12. Greenfield and Pritchard.[1c] Tfunada and Shimamura.[1d] Chasnoff.[5] Maltby and Schmidt.[2]

# ELECTROENCEPHALOGRAM IN THE PITRESSIN HYDRATION TEST FOR EPILEPSY

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AND
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## THE PROBLEM

IN A LARGE number of patients with alterations of consciousness and convulsive seizures there is difficulty in establishing the diagnosis of epilepsy because the seizures cannot be observed and the electroencephalogram is not sufficiently abnormal to warrant a probable diagnosis of paroxysmal disorder. The necessity of arriving at a diagnosis with reasonable certainty is particularly great in military neuropsychiatry. Army regulation requires confirmation of the history by a medical officer, who must witness a seizure or an abnormal electroencephalogram. Concerning such witnessing of a seizure, Roseman [1] pointed out how rarely a qualified observer has the opportunity to observe a convulsive seizure in the wards of a military hospital. As to the value of the electroencephalogram, Gibbs, Gibbs and Lennox [2] found that in a series of 730 adult epileptic patients the electroencephalogram gave little diagnostic aid in 47.1 per cent.

This problem is of long standing, and many technics have been evolved to prove or disprove the diagnosis of epilepsy, the most useful of which is the pitressin hydration test developed by McQuarrie and Peeler.[3] They showed that grand mal seizures can be induced within twelve to forty-eight hours in epileptic children by giving water while maintaining effective pituitary antidiuresis. Alteration of the colloids and electrolytes in the brain was considered the essential factor. Subsequent work by Jacobsen,[4] also on children, and by Clegg and Thorpe,[5]

1. Roseman, E.: The Epileptic in the Army, Am. J. Psychiat. **101**:349-354 (Nov.) 1944.

2. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Electroencephalographic Classification of Epileptic Patients and Control Subjects, Arch. Neurol. & Psychiat. **50**:111-128 (Aug.) 1943.

3. McQuarrie, I., and Peeler, D. B.: The Effects of Sustained Pituitary Antidiuresis and Forced Water Drinking in Epileptic Children: A Diagnostic and Etiologic Study, J. Clin. Investigation **10**:915-940 (Oct.) 1931.

4. Jacobsen, A. W.: The Pitressin Test in Epilepsy, New York State J. Med. **34**:506-509 (June 1) 1934.

5. Clegg, J. L., and Thorpe, F. T.: Induced Water Retention in Diagnosis of Idiopathic Epilepsy, Lancet **1**:1381-1382 (June 15) 1935.

Hilger, Mueller and Freed,[6] Garland and associates;[7] Blyth[8] and others gave further support to the validity of the test. Garland and associates[7] reviewed the literature to 1943 and found that various observers had reported 10 to 100 per cent efficacy for this test, with approximately 40 per cent positive results in series excluding children. He suggested studying the pitressin hydration test in conjunction with electroencephalography. Gibson[9] combined the pitressin hydration test with hyperpnea and found a positive reaction in 75 per cent of epileptic patients. However, Clegg and Thorpe[5] concluded that, although the pitressin hydration test is of definite value in arriving at a diagnosis of epilepsy in doubtful cases, no fit may be induced when the patient has seizures infrequently. Stone and Chor[10] presented the divergent opinion that a high fluid intake with or without the addition of an antidiuretic did not produce an increase in the incidence of convulsions in their group of adult epileptic patients. Further, their biochemical studies led them to doubt the efficacy of the hydration technic. The work of several other observers, who also felt that the pitressin hydration test is of doubtful value, was cited. A review of the literature failed to reveal any study of the pitressin hydration test in conjunction with electroencephalography except possibly by Allen,[11] whose work on dogs was discontinued after one tracing was made.

In our material the pitressin hydration test was applied to patients with a reliable history of convulsive seizures whose electroencephalograms were normal. In this group, which consisted of relatively mildly affected subjects, seizures were induced infrequently. It was then decided to examine the electroencephalogram of these patients at the conclusion of the pitressin hydration test in an attempt to discover changes of possible diagnostic significance. Further, the electroencephalograms of 11 patients with a diagnosis of fainting and those of 10 controls were studied in similar circumstances. The electroencephalographic changes will be reported.

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6. Hilger, D. W.; Mueller, A. R., and Freed, A. E.: The Pitressin Hydration Test in the Diagnosis of Idiopathic Epilepsy, Mil. Surgeon **91**:309-313 (Sept.) 1942.

7. Garland, H. G.; Dick, A. P., and Whitty, C. W. M.: Water-Pitressin Test in Diagnosis of Epilepsy, Lancet **2**:566-569 (Nov. 6) 1943.

8. Blyth, W.: The Pitressin Diagnosis of Idiopathic Epilepsy, Brit. M. J. **1**:100-102 (Jan. 23) 1943.

9. Gibson, P. L.: Pitressin Hyperpnea Test and Epilepsy, J. Roy. Nav. M. Serv. **23**:334-338 (Oct.) 1937.

10. Stone, T. T., and Chor, M.: Water Metabolism in Relation to Convulsions, Arch. Neurol. & Psychiat. **38**:798-817 (Oct.) 1937.

11. Allen, F. M.: Spontaneous and Induced Epileptiform Attacks in Dogs, in Relation to Fluid Balance and Kidney Function, Am. J. Psychiat. **102**:67-73 (July) 1945.

## MATERIAL

*Patients with Convulsive Seizures* (1 to 12, table 1).—All patients in this group were thought to have idiopathic epilepsy, grand mal type. Only patients with normal electroencephalograms were included. Some of the characteristic symptoms and electroencephalographic findings are indicated in table 1. Eleven patients reported generalized convulsive seizures, and all, loss of consciousness and amnesia. In 6 of the 12 patients seizures were observed by a medical officer. As in most patients seen in military hospitals, the average frequency of seizures was low.

*Patients with Syncopal Attacks* (13 to 23, table 2).—For patients 13 to 19 the diagnosis of hysterical fainting was made in accordance with the diagnostic criteria as outlined by Romano and Engel.[12] For patients 20, 21 and 22 the diagnosis was not certain, and there was some doubt as to whether these patients were epileptic. In the case of patient 23 it was felt that the old diagnostic term of hysteroepilepsy fitted the picture best, as the patient had a hysterical personality and seizures characterized by loss of consciousness without convulsions. All electroencephalograms prior to pitressin hydration in this group were normal.

*Controls* (24 to 33, table 3).—For 7 of these patients the diagnosis was mild post-traumatic encephalopathy manifested by headache; for 1, postmeningitic cephalalgia, and for 2, anxiety state. Here, too, the electroencephalograms taken prior to pitressin hydration were normal.

All patients were subjected to a complete physical and neurologic examination, with attention to sensitivity of the carotid sinus. Laboratory procedures included a blood count, examination of the urine, a Wassermann test and roentgenographic examination of the skull. The patients in groups 1 and 2 had, in addition, a lumbar puncture, with determination of pressure and study of the spinal fluid, and a carbohydrate tolerance test. All findings were noncontributory except in a negative sense.

## METHOD

*The Pitressin Hydration Test.*—The technic described by Garland was considered to be simple, effective, safe and in conformity with the technics used by workers in similar studies and was therefore followed. A regular diet was given. The patients were kept in bed for the day of the test and twenty-four hours thereafter. Sideboards were used. The patient was weighed at 6:55 a. m. on the day of the test, after emptying the bladder, and then every three hours. The intake and output of fluids were charted. The blood pressure was determined every two hours. A pint (473 cc.) of water was given hourly for eleven hours, starting at 7:00 a. m. Pitressin was given hourly, starting at 10:00 a. m., according to the following dosage: 0.2, 0.3 and 0.4 cc., and then 0.5 cc. for four doses. The electroencephalogram was made at approximately 6 p. m. If a convulsion occurred, the test was stopped immediately and phenobarbital, 1½ grains (0.097 Gm.), administered.

*Electroencephalographic Technic and Classification.*—The electroencephalogram was determined by the standard technic.[13] A Grass encephalograph was used.

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12. Romano, J., and Engel, G. L.: Studies of Syncope: III. Differentiation Between Vasodepressor and Hysterical Fainting, Psychosom. Med. **7**:3-15 (Jan.) 1945.

13. Electroencephalography: Operative Technique and Interpretation, United States War Department, Technical Bulletin (TB Med 74), Washington, D. C., Government Printing Office, July 27, 1944.

TABLE 1.—*Effect on Electroencephalogram of Pitressin Hydration Test in Patients with Clinical Diagnosis of Epilepsy*

| Patient No. | Age | Seizures Reported | Seizures Observed | Frequency of Seizures | Age (Yr.) at Onset of Seizures | Convulsions | Unconsciousness | Tongue Biting | Incontinence | Family History of Epilepsy | EEG Type * | | Comment |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | Before Pitressin Hydration | After Pitressin Hydration | |
| 1 | 22 | Yes | Yes | Infrequent | 10 | Yes | Yes | Yes | Yes | + | N<br>N<br>N<br>F.1 | F.2<br>F.2<br>F.2 | Seizure 5 hr. after hydration; marked change persisted 1 week |
| 2 | 21 | Yes | Yes | 2 in 9 yr. | 11 | Yes | Yes | Yes | No | + | L.V.F.<br>N | F.1<br>F.1 | Slight change |
| 3 | 23 | Yes | Yes | Infrequent | 19 | Yes | Yes | Yes | No | — | N | P.M. | Marked change; seizure 6 days after hydration |
| 4 | 21 | Yes | No | Infrequent | Early life | No | Yes | No | No | + | N<br>N | S.1 | Slight change |
| 5 | 19 | Yes | No | Total 5 | 14 | Yes | Yes | Yes | No | + | N | S.1 | Slight change |
| 6 | 25 | Yes | Yes | 4 in 4 mo. | 24 | Yes | Yes | Yes | Yes | — | N | S.1 | Slight change |
| 7 | 20 | Yes | No | 5 in 18 mo. | 19 | Yes | Yes | No | No | + | N | Psy. | Marked change |
| 8 | 24 | Yes | Yes | 2 in 2 mo. | 24 | Yes | Yes | Yes | No | — | N<br>N | F.1 | Slight change |
| 9 | 25 | Yes | Yes | Infrequent | 16 | Yes | Yes | Yes | No | — | N | F.1 | Slight change |
| 10 | 28 | Yes | No | 7 in 9 yr. | 19 | Yes | Yes | Yes | Yes | — | N | N | No change except 2 short 18-24 per sec. bursts |
| 11 | 22 | Yes | Yes | 2 yr. | Childhood | Yes | Yes | Yes | Yes | + | N<br>N | N | No change |
| 12 | 24 | Yes | Yes | Infrequent | 18 | Yes | Yes | No | Yes | — | N | N | No change; seizure 6 hr. after hydration |

* In this table, and in the accompanying tables, N indicates a normal electroencephalogram; F.1, slightly fast activity; F.2, very fast activity; L.V.F., low voltage fast activity; P.M., petit mal type, and S.1, slightly slow activity.

The electrical activity of the frontal, motor, temporal and occipital areas was recorded with monopolar leads. The classification of Gibbs, Gibbs and Lennox was followed. For our comparisons this classification, although based on subjective criteria, was deemed satisfactory; actually, more objective methods are cumbersome and do not yield more useful results. The classification as described by Gibbs, Gibbs and Lennox [2] includes the following categories:

A. Paroxysmal
   1. Petit mal variant—P.M.V.
   2. Petit mal type—P.M.
   3. Psychomotor type—Psy.
   4. Grand mal type—G.M.
   5. Spikes—Sp.

B. Slow activity
   1. Very slow—S.2
   2. Slightly slow—S.1

C. Normal activity
   1. From 8½ to 12 waves per second
   2. Low voltage fast—L.V.F.

D. Fast activity
   1. Slightly fast—F.1
   2. Very fast—F.2

Records taken before and after pitressin hydration were compared primarily as to any change in frequency and character of the brain waves. Deviations were expressed in terms of the classification of Gibbs, Gibbs and Lennox.[2] Changes from normal to fast (F. 1) or slow (S. 1) frequencies were classified as "slight." Changes from normal to very fast (F. 2), to very slow (S. 2) or to paroxysmal (petit mal, petit mal variant, psychomotor, grand mal and spikes) dysrhythmias were counted as "marked."

## OBSERVATIONS

It was found that the pitressin hydration test was in general well tolerated by the patients.

In the entire series convulsive seizures occurred as follows: In patient 1 a grand mal seizure occurred in the fifth hour of the test; in patient 12 six hours after termination of hydration, and in patient 3, six days (!) after hydration. All these patients were presumed to be epileptic. Side reactions were similar to those observed by previous workers and consisted of pallor, occasional abdominal cramps, occasional vomiting and occasional headache, none of which was severe enough to cause suspension of the procedure. The blood pressure did not vary significantly except in patient 24, in whom it rose from normal to 210 systolic and 110 diastolic in the eighth hour of the test, at which time the test was discontinued. This elevation was accompanied with headache and dizziness. Phenobarbital was administered, after which the blood pressure became normal in a short period. In the case of patient 16 the test was discontinued in the seventh hour for the sake of safety because at that time he suddenly sat up in bed and complained of queer feelings. There was no loss of consciousness. The blood pressure was normal. The electroencephalogram taken immediately was normal. It was felt that this was not an epileptic manifestation.

A positive water balance was uniformly obtained, as evidence by a diminution of urinary output as compared with the fluid intake and by a gain in weight (average 5.3 pounds [2.4 Kg.]).

In the group of patients with convulsive seizures (table 1), 3 of 11 patients showed pronounced changes in the electroencephalogram after

pitressin hydration; the record of patient 1, which was previously normal, showed very fast activity; the record of patient 3, which was normal, contained some petit mal waves after the test; and the record of patient 7 changed from a normal to a psychomotor pattern. For 6 patients the alterations were characterized as slight, as manifested by a change from a normal record before the test to one with fast frequencies for 3 patients and to one with slow frequencies for 3 patients. The record of patient 10 showed only a slight change, which consisted of two short bursts of 18 to 24 per second waves of medium voltage in an otherwise normal record. In the records of patients 11 and 12 no change was noted in spite of the fact that the latter had two grand mal seizures, witnessed by a nurse about five hours after the recording.

In the second group of patients, who had fainting attacks (table 2), no changes in the electroencephalogram were noted after hydration

TABLE 2.—*Effect on Electroencephalogram of Pitressin Hydration Test in Patients with Syncope*

| Patient No. | Diagnosis | Type of EEG: Before Pitressin Hydration Test * | Type of EEG: After Pitressin Hydration Test | Comment |
|---|---|---|---|---|
| 13 | Vasodepressor syncope | N (4) | N | No change |
| 14 | Hysterical syncope | N (4) | N | No change |
| 15 | Hysterical syncope | N (3) | N | No change |
| 16 | Hysterical syncope | N | N | No change; hydration suspended † |
| 17 | Hysterical syncope | N (2) | N | No change |
| 18 | Hysterical syncope | N (2) | N | No change |
| 19 | Hysterical syncope | N | N | No change |
| 20 | Psychopathic personality ? epilepsy | N (2) | N | No change |
| 21 | Hysterical syncope ? epilepsy | N | N | No change |
| 22 | Psychopathic personality ? epilepsy | N (2) | N | No change |
| 23 | ? Hysteroepilepsy | N | F.1 | Slight change |

* Figures in parentheses refer to the number of records made.
† Bizarre behavior in the seventh hour of the test.

except for that of patient 23, in which there was a slight change. This patient was a 23 year old private first class who was hospitalized for nervousness accompanied with dizzy spells, black-outs and a sensation described as "electricity" in the cervical and occipital regions, all of three months' duration. There was no history of convulsions, incontinence or tongue biting. The soldier was amnesic for the period of unconsciousness. He gave the impression of a hysterical personality, with much anxiety. The family history was normal, and neurologic examination and laboratory tests revealed nothing significant. The diagnosis in this case remained obscure, since no definite psychogenic explanation could be found to account for his loss of consciousnes on a hysterical basis.

In the group of control patients (table 3) no alteration in the electroencephalogram was noted after hydration except as follows:

Patient 24 showed a change in the record from low voltage fast to fast (F1) activity. In this patient the hydration was complicated by hypertension (210 systolic and 110 diastolic). Patient 31, for whom a diagnosis of postmeningitic cephalalgia was established, showed a slight change in that a few 12 to 14 per second and a few 7 to 8 per second brain waves were noted after hydration.

## COMMENT

According to Gibbs, Gibbs and Lennox, the use of the electroencephalogram alone permitted confirmation of the diagnosis of epilepsy in only 39 per cent of cases (paroxysmal records). In 32 per cent records showing fast (F. 1) or slow (S. 1) activity gave only supporting evidence, and in 13 per cent of epileptic patients the electroencephalogram

TABLE 3.—*Effect on Electroencephalogram of Pitressin Hydration Test in Control Subjects*

| Patient No. | Diagnosis | Type of EEG: Before Pitressin Hydration Test | Type of EEG: After Pitressin Hydration Test | Comment |
|---|---|---|---|---|
| 24 | Post-traumatic encephalopathy | L.V.F. | F.1 | Test suspended because of hypertension * |
| 25 | Post-traumatic encephalopathy | N | N | No change |
| 26 | Anxiety state | N | N | No change |
| 27 | Cephalalgia | N | N | No change |
| 28 | Post-traumatic encephalopathy | N | N | No change |
| 29 | Anxiety state | N (2 records) | N | No change |
| 30 | Post-traumatic encephalopathy | N | N | No change |
| 31 | Postmeningitic cephalalgia | N | ? N | Very slight change † |
| 32 | Post-traumatic encephalopathy | N | N | No change |
| 33 | Post-traumatic encephalopathy | N | N | No change |

* The blood pressure rose to 220 systolic and 110 diastolic in the eighth hour of the test.
† The change consisted in the appearance of a few 12 to 14 and 7 to 8 per second bursts.

was normal. Roseman [1] found that 21 per cent of his 364 patients had normal records. Of our 120 patients, the records of 39.2 per cent showed normal, borderline normal or low voltage fast activity. The records with fast (F. 1) and slow (S. 1) potentials comprised 18 per cent. Thus, the electroencephalogram alone gave little diagnostic aid in 57.2 per cent of our patients. The fact that the electroencephalogram tends to show fewer abnormalities in military epileptic patients, who by and large have a mild form of the disease and have previously been screened, had been observed by O'Leary.[14] This consideration makes it even more desirable to find other objective technics in order to arrive at a diagnosis of epilepsy in patients whose electroencephalogram is not decisive. This consideration led us to use the pitressin hydration test in combination with electroencephalographic observation.

14. O'Leary, J.: Verbal communication to authors.

Pitressin hydration induces seizures in a variable percentage of epileptic patients, probably depending on the degree of hydration. This is attributed to the alteration of colloids and electrolytes in the tissues of the brain. The work of Fremont-Smith, Merritt and Lennox [15] confirmed this hypothesis and showed that the mechanical theory is untenable, since the cerebrospinal fluid pressure after hydration was found to be only slightly increased and the cerebrospinal fluid pressures at the time of seizures were within normal limits.

The pitressin hydration technic is not without danger, particularly when a large dose of the drug is administered. Deaths have been reported in the literature in the older age groups. Young and otherwise vigorous adults seem to tolerate the procedure as outlined in this report without serious difficulty. More drastic hydration does not seem warranted. Careful selection of cases and caution are indicated.

Our electroencephalographic findings suggest that pitressin hydration causes a dysrhythmia in epileptic patients whose electroencephalograms were previously normal. We noted pronounced changes in the records of 3 and slight changes in the records of 6 of the 12 patients in the epileptic group. The 3 remaining patients showed no significant change. Such changes were shown by only 1 of 11 patients with fainting attacks, in group 2, and by 2 of 10 control subjects. This difference is even more striking when we consider that patient 23, in group 2, who showed slight changes, may well have been epileptic, and that in patient 24 hydration was complicated by an abrupt and severe elevation of the blood presure. Patient 31, in the control group, who showed very slight changes, had recently recovered from meningococcic meningitis, with possible, though undetectable, cerebral change.

Our results at least seem to encourage a similar study on a larger group of patients. Tentatively, it may be said that cerebral hydration induces cerebral dysrhythmia in patients with epilepsy. In normal persons and in patients with fainting attacks (vasodepressor and hysterical syncope) few electroencephalographic changes were induced. A moderate and well tolerated degree of pitressin hydration seems to induce electroencephalographic changes more frequently than actual seizures in adult epileptic patients with a mild form of the disease, if one may judge from such a small number of cases. We believe that electroencephalographic observations before and after pitressin hydration add to the diagnostic significance of the test and aid in the differential diagnosis of the paroxysmal disorders and syncopes.

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15. Fremont-Smith, F.; Merritt, H. H., and Lennox, W. G.: Relationship Between Water Balance, Spinal Fluid Pressure and Epileptic Convulsion, J. Nerv. & Ment. Dis. **76**:176-179 (Aug.) 1932.

SUMMARY

The pitressin hydration test in conjunction with electroencephalographic study was applied to 12 patients for whom a clinical diagnosis of epilepsy was made, 11 patients with psychogenic fainting and 10 control subjects. All patients had normal electroencephalograms prior to hydration.

Convulsive seizures occurred in the epileptic group as follows: in 1 patient during the test, in 1 shortly after the test and in 1 six days later.

The electroencephalograms of 9 of 12 patients of the epileptic group showed changes after pitressin hydration (3 patients had marked changes, and 6 patients, slight changes). In the group consisting of patients with psychogenic disturbance of consciousness slight changes occurred in the record of 1 of 11 patients. In the control group, 2 of 10 subjects showed slight changes. For 1 of these subjects a diagnosis of postmeningitic state was made. The other had a sharp rise in his blood pressure after hydration.

The findings are discussed; and, although the number of observed cases was small, the results are thought to be significant and of some value in differentiating epilepsy from hysterical and vasodepressor disturbances of consciousness.

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# ABDOMINAL RIGIDITY

## A Symptom of Concussion of the Spinal Cord

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IT HAS been common practice to include all the injuries to the spinal cord arising out of indirect violence in the one term "spinal concussion." For the purpose of this paper, the more definite term "concussion of the spinal cord" seems better and will be used. It signifies the presence in the spinal cord of a physiologic state similar to that in the cerebrum when the term "cerebral concussion" is used. In concussion of the spinal cord a transitory functional, and perhaps structural, disturbance of the spinal cord is incurred consequent to indirect trauma to the cord. This definition emphasizes the functional reversibility of the injury to the cord and makes it evident that recovery occurs in a relatively short time, that is, from a few hours to a few days. The reports in the literature and my experience in World War II indicate that functional recovery should occur in less than two weeks, more likely within ten days. It is presumed that when loss of function persists longer than ten days the injury to the spinal cord is of a structural and more serious type or degree than concussion.

The greatly confused subject of "spinal concussion" [1] in general has been the topic of considerable controversy and speculation for at

Dr. Abbott has received his discharge from the service and is now located in Rochester, Minn.

1. Most writers include any type of injury to the spinal cord as a result of indirect trauma under the term "spinal concussion," "commotio spinalis" or *Rückenmarkserschütterung,* of the German writers. The papers of H. Obersteiner (Ueber Erschütterung des Rückenmarkes, Med. Jahrb., 1879, pp. 531-562; abstracted, Schmidt's Jahrb. **186**:236-237, 1880), J. Lhermitte (Étude de la commotion de la moelle, Rev. neurol. **1**:210-239 [Feb.] 1932), G. B. Hassin (Concussion of the Spinal Cord: A Case with Clinical Picture of Amyotrophic Lateral Sclerosis, Arch. Neurol. & Psychiat. **10**:194-211 [Aug.] 1923), O. Marburg (Die traumatischen Erkrankungen des Gehirns und Rückenmarks: B. Die traumatischen Erkrankungen des Rückenmarks, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, vol. 11, pp. 100-153), H. Claude and J. Lhermitte (Étude clinique et anatomo-pathologique de la commotion médullaire directe par projectiles de guerre, Ann. de méd. **2**:479-506, 1915) and C. Davison (General Pathological Considerations in Injuries of the Spinal Cord, in Brock, S.: Injuries of the Skull, Brain and Spinal Cord: Neuro-Psychiatric, Surgical and Medico-Legal Aspects, Baltimore, Williams & Wilkins Company, 1940, pp. 453-485), among innumerable others, all exemplify the broad and nonspecific use of these terms.

least two centuries, and little enlightenment has resulted. In the last century Erichsen [2] reviewed the subject thoroughly; and, like all other investigators of his time and many since, he confused many different types of traumatic lesions of the spinal cord with unrelated degenerative diseases, neuroses ("railway spine") and inflammatory processes. However, he suggested that a "molecular disturbance" [3] in the spinal cord was the fundamental cause of the immediate loss of function and of other symptoms subsequent to trauma. Just what he meant by "molecular disturbances" is not clear, but he implied that minor intracellular (or fiber) structural changes took place in the neurons. If this interpretation of his meaning is correct, his hypothesis is not unlike present conceptions concerning the histologic and physiologic changes accompanying cerebral concussion.

Recent investigations have pointed toward a structural basis for the clinical symptoms of true concussion of the spinal cord. Groat and co-workers [4] observed definite cellular changes in the spinal cords of cats which had been subjected to blows of the type that produce concussion. These cellular changes were characterized by chromatolysis involving principally the "interneurons of large and intermediate size of both dorsal and ventral grey columns." The long descending and ascending fiber tracts were also involved,[5] as were the lower motor

2. Erichsen, J. E.: On Concussion of the Spine, Nervous Shock, and Other Obscure Injuries of the Nervous System in Their Clinical and Medico-Legal Aspects, revised ed., New York, Bermingham & Co., 1882, p. 93.

3. Hassin gave credit to Obersteiner for introducing the term "molecular" change as the essence of spinal concussion. However, it appears that Erichsen [2] (ed. 1, New York, William Wood & Company, 1875) published his book four years before Obersteiner's paper appeared (1879).

4. Groat, R. A.; Rambach, W. A., Jr., and Windle, W. F.: Concussion of the Spinal Cord: An Experimental Study and Critique of the Use of the Term, Surg., Gynec. & Obst. **81**:63-74 (July) 1945.

5. It is not intended in this paper to consider details of theories about commotio spinalis or the minutiae of its pathology. The results of the recent, and more accurately controlled, experimental work of Groat and his co-workers, however, seem more closely to coincide with the clinical aspect of concussion of the spinal cord than the results of any previously reported experimental or clinicopathologic study. These previous studies have been summarized by Groat and his associates [4] and in the papers of W. G. Spiller (A Critical Summary of Recent Literature on Concussion of the Spinal Cord with Some Original Observations, Am. J. M. Sc. **118**:190-198 [Aug.] 1899), J. Lhermitte (Étude de la commotion de la moelle, Rev. neurol. **1**:210-239 [Feb.] 1932), G. B. Hassin (Concussion of the Spinal Cord: A Case with Clinical Picture of Amyotrophic Lateral Sclerosis, Arch. Neurol. & Psychiat. **10**:194-211 [Aug.] 1923), C. Davison (General Pathological Considerations in Injuries of the Spinal Cord, in Brock, S.: Injuries of the Skull, Brain and Spinal Cord: Neuro-Psychiatric, Surgical and Medico-Legal Aspects, Baltimore, Williams & Wilkins Company, 1940, pp. 453-485) and others.

neurons, but to a much less extent. These changes were proportional to the severity of the concussion. Edema also has been observed. In the light of the definition of concussion of the spinal cord given, it is unlikely that petechial hemorrhages and focal necrosis, as described by certain investigators, belong to the syndrome of concussion of the spinal cord. Changes similar to those produced by electrical phenomena accompanying cerebral concussion, namely, intense excitation, after-discharge and extinction, as described by Walker and associates,[6] possibly may exist in the cord consequent to concussion. If concussion of the spinal cord can be explained on the same basis as cerebral concussion, it may be caused in part by a breakdown of the polarized cell membranes of many spinal neurons, thus discharging intercollated and other neurons.[7]

In war concussion of the spinal cord is common consequent to the striking of vertebral bodies or processes with a missile. In such injuries concussion of the spinal cord may occur even if the spinal column is not fractured. Perforation of the body of a vertebra frequently causes concussion or contusion of the cord. A blow or a fall on the back without fracture of the spinal column likewise may be the cause of concussion of the spinal cord. The damage inflicted on the cord by an indirect injury resulting from a blow or fall has been well described by Holmes,[8] who saw many such injuries in World War I, and by many other authors. It varies from transitory loss of function without evidence of gross damage to complete transection of the cord.

Clinically the symptoms of concussion of the spinal cord vary greatly. Most commonly motor and sensory function at and below the site of concussion of the cord is lost temporarily. The intensity and duration of the paralysis vary, but it always lasts less than two weeks. Kislow,[9] who had studied an unusually large number of spinal injuries in the Russian army, aptly pointed out that in cases of concussion of the spinal cord the site of the gunshot wound, the vertebral damage and the lesion of the cord do not have a direct relationship. Whether this absence of relationship is due to spinal shock (von Monakow's

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6. Walker, A. E.; Kollros, J. J., and Case, T. J.: The Physiological Basis of Concussion, J. Neurosurg. **1**:103-116 (March) 1944.

7. Groat and his associates[4] recognized this possibility but were unable to find experimental evidence to support this theory as applied to the spinal cord.

8. Holmes, G.: The Goulstonian Lectures on Spinal Injuries of Warfare: I. The Pathology of Acute Spinal Injuries, Brit. M. J. **2**:769-774 (Nov. 27) 1915; II. The Clinical Symptoms of Gunshot Injuries of the Spine, ibid. **2**:815-821 (Dec. 4) 1915; III. The Sensory Disturbances in Spinal Injuries, ibid. **2**:855-861 (Dec. 11) 1915.

9. Kislow, V. A.: Clinical Peculiarities of War Wounds of the Spinal Cord, abstracted, Bull. War Med. **4**:705 (Aug.) 1944.

"diaschisis"), as Kislow said, to violent changes in the circulation of spinal fluid, or to vascular stasis with ischemia is not certain. In Kislow's group of patients the motor paralysis was spastic in 35 per cent and flaccid in 65 per cent. He further stated that 97 per cent of the patients recovered in from two to thirteen days when the motor paralysis was not due to destruction of the cord. This suggests that this group suffered principally from true concussion of the cord. Sensory recovery, he noted, usually tarried behind motor recovery. Others have reported similar findings which emphasize that spasticity is a common clinical symptom of concussion of the spinal cord. It is also of interest that in cats with experimentally induced spinal concussion the hindlimbs were frequently extended in tonic spasm. Here, again, the symptoms were transitory; and if the symptoms were consequent to structural disturbances (chromatolysis and others), these cellular changes were probably reversible.

## CLINICAL FINDINGS IN SEVEN CASES

In evacuation hospitals in the combat zone in the Southwest Pacific Theater of Operations, 7 out of more than 100 soldiers examined by me because of acute injuries to the spinal cord presented certain interesting symptoms of spinal concussion. These patients were seen from one to five hours after injury had occurred, and all of them had abdominal rigidity with mild to severe spasticity in extension of the lower extremities and varying degrees of sensory paralysis up to the level of the lesion. The injuries were all the result of bullet, shell or bomb fragment wounds of the back in the thoracic and lower cervical regions. Four patients presented roentgenographic evidence of fractures of the laminas or spinous processes without comminution or displacement of bone. Although the roentgenograms of the other 3 patients did not show any evidence, fractures may have been present, for stereoscopic views were not available. The spinal fluid of 5 patients was entirely normal, and that of 2 patients contained a few red blood cells. These 2 patients, who also had fractures, may be considered to have had contusion of the cord, although the clinical course of these men varied but little from that in the others.

All the patients gave a history of complete loss of motor and sensory function in the lower extremities and approximately the lower half of the trunk. This was present from a few minutes to four hours after injury and was followed by a gradual return of sensory function, usually accompanied with paresthesia. Coincident with the return of sensory function, all 7 patients complained of increasing abdominal pain with varying degrees of pain in the lower extremities. Because of this abdominal pain, nearly all the patients had been seen by general surgeons, who asked for neurosurgical consultation because of the lack

of evidence of penetrating abdominal wounds or of direct or indirect injury to the abdomen, pleura or lung.

The neurologic examination disclosed both sensory and motor deficits affecting the lower extremities and the trunk. The sensory changes varied from pronounced to mild; hypesthesia and, frequently, dysesthesia and paresthesia were prominent. The sensory changes usually extended irregularly to the lower or middle part of the thoracic region. Sensations of pain and temperature were much more severely impaired than sensations of touch and pressure. Postural sense was poor. Mild to severe motor paralysis of the lower extremities with varying degrees of spasticity in extension was present, although all the patients had experienced complete paralysis of the lower extremities immediately after the injury. The abdominal muscles were likewise spastic, actually rigid, and no one quadrant was affected more than others. Although the patients complained of abdominal pain, sometimes more severe on one side than on the other, localized tenderness was not demonstrable. The abdominal rigidity was not unlike that found with peritoneal irritation from various causes, but no rebound tenderness was present and other evidence of intra-abdominal disease or injury was lacking.

The cremasteric reflexes were sluggish or absent, while the superficial abdominal reflexes were not elicited except in 1 patient, and in this patient they were unequal on the two sides and sluggish. The abdominal muscle reflexes, examined in 2 patients, were bilaterally hyperactive. The state of the patellar and tendo achillis reflexes varied greatly, from absence (4 patients) to hyperactivity (1 patient); but when present they were unequal. These patients were not followed closely enough throughout the ensuing hours and days to warrant any conclusions as to the significance of these irregularities. The plantar responses were absent in 3, "normal" in 1 and "slightly positive" in 3. Rotation of the head failed to induce any change in the position or in the intensity of the spasticity of the lower extremities in any of these 7 patients.

In all these patients the symptoms were transitory. The motor paralysis (paralysis in extension or extensor spasms) and abdominal rigidity nearly or completely disappeared in from two to forty-eight hours. In no instance did abdominal rigidity persist longer than forty-eight hours. The motor weakness completely disappeared in forty-eight hours in 5 patients, while in the 2 patients who had blood in the cerebrospinal fluid the paralysis had improved notably in forty-eight hours. By the fourth day these 2 patients were able to walk without assistance, and neurologic examination disclosed only slight weakness and revealed that the tendon reflexes and plantar responses were within normal limits. These patients were then evacuated to hospitals farther back and could not be followed.

COMMENT

The problems of incomplete section of the spinal cord have been studied extensively, so that it may be stated that "paraplegia in extension is common in spinal lesions and bears evidence that the spinal cord has not been completely severed." [10] Ranson, Muir and Zeiss,[11] in experiments in which cats were used, were able to reproduce the equivalent of paraplegia in extension by producing lesions involving the dorsal two thirds of the spinal cord. These experimental results suggest that integrity of the tracts in the anterior and anterolateral portions of the cord is necessary for paraplegia in extension to occur. Studies on decerebrate rigidity by Sherrington,[12] Magnus,[13] Weed,[12] Keller [12] and others [14] have thrown further light on the problem of paraplegia in extension caused by lesions of part of the cord. Their experiments suggest that decerebrate rigidity must depend on the interruption of extrapyramidal pathways. Fulton, Liddell and Rioch [15] demonstrated that isolated destruction of the vestibular nuclei abolished rigidity in decerebrate preparations, thus indicating that integrity of the vestibular nuclei is necessary in the production of rigidity.

In attempting to explain the physiology of the syndrome of concussion of the spinal cord, it is necessary to eliminate what might be called "local causes" of the abdominal rigidity. Only 3 of the 7 patients had any type of wound of the abdomen, and these were minor and certainly would not be considered capable of producing generalized abdominal symptoms. Wounds of the pleura and lung, which are likewise known to produce abdominal rigidity, were also eliminated as possible etiologic factors. Blood as an irritant to the spinal roots was a possible cause of the abdominal rigidity in only 2 patients. The problem, therefore, appears to be one of determining what structures or tracts in the spinal cord were functionally interrupted. From the evidence presented by these 7 patients, it would appear that the concussion temporarily interrupted the extrapyramidal tracts in the cord (figure). It is also necessary to assume that the vestibular tracts were functionally intact.

10. Fulton, J. F.: Physiology of the Nervous System, ed. 2, New York, Oxford University Press, 1943, p. 140.

11. Ranson, S. W.; Muir, J. C., and Zeiss, F. R.: Extensor Tonus After Spinal-Cord Lesions in the Cat, J. Comp. Neurol. **54**:13-33 (Feb.) 1932.

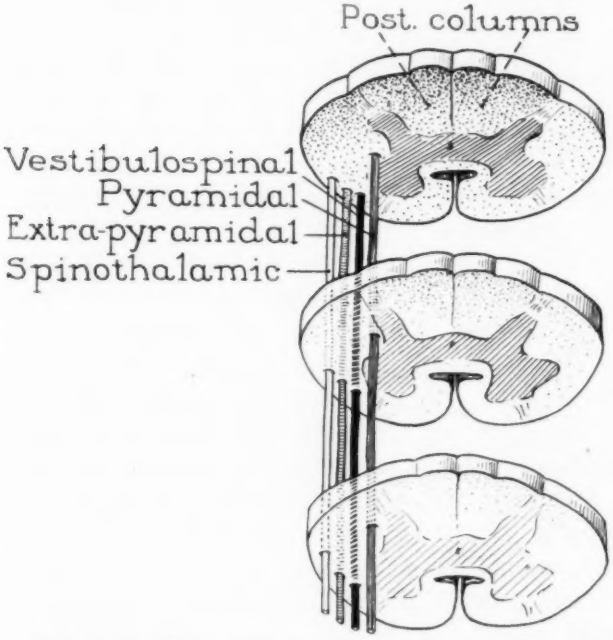
12. Cited by Fulton,[10] chap. 8, pp. 118-162.

13. Magnus, R., cited by Fulton,[10] chap. 8, pp. 118-162.

14. Bazett, H. C., and Penfield, W. G.: A Study of the Sherrington Decerebrate Animal in the Chronic as well as the Acute Condition, Brain **45**:185-265 (Oct.) 1922.

15. Fulton, J. F.; Liddell, E. G. T., and Rioch, D. McK.: The Influence of Experimental Lesions of the Spinal Cord upon the Knee-Jerk: I. Acute Lesions, Brain **53**:311-326 (Oct.) 1930; The Influence of Unilateral Destruction of the Vestibular Nuclei upon Posture and the Knee-Jerk, ibid. **53**:327-343 (Oct.) 1930.

In addition to the extrapyramidal tracts, the pyramidal and spinothalamic tracts were interrupted functionally to various degrees. The symptom of abdominal rigidity was noted while these tracts were recovering, though severely involved. The posterior columns were also affected but to a less degree than the lateral spinothalamic tracts. Thus, a lesion of part of the spinal cord produced rigidity in extension of the lower extremities, sensory impairment and spasticity (rigidity) of the abdominal muscles; the last-named probably is another manifestation of extensor spasticity. Thus, below the level of the spinal lesion a condition exists which resembles a decerebrate state.




Schematic diagram of the tracts of the spinal cord partially or completely but temporarily interrupted consequent to concussion of the spinal cord. Spasticity in extension of the lower extremities and abdominal rigidity result.

## SUMMARY

The term "concussion of the spinal cord" is limited in this paper to a transitory syndrome following indirect injury to the spinal cord. Seven cases are described in which the syndrome of transitory sensory paralysis of the lower extremities with involvement of the trunk into the thoracic region was accompanied by abdominal rigidity and paralysis in extension of the lower extremities. No clinical evidence of gross damage to the spinal cord was found in 5 cases, and in 2 a small quantity of blood was observed in the spinal fluid. All the patients recovered. It is considered that the symptoms referable to the lesion may be due to a so-called molecular disturbance and that the reversible

structural changes within the nerve cells and fibers, associated with probable changes in electrical conductivity and excitation, are not unlike those in cerebral concussion. A brief review of the physiology of the spinal cord in relation to paraplegia in extension suggests that the syndrome resembles that of the decerebrate state, for it is manifest below the level of the spinal injury and is due to involvement of the extrapyramidal pathways without interruption of the vestibulospinal tracts.

The Mayo Clinic, Rochester, Minn.

# Obituaries

## WALTER DE WITT SHELDEN, M.D.
### 1870-1946

It may be said that a good teacher or a good diagnostician never mistakes information for understanding or fancy for fact. Dr. Shelden did neither and was both. After his acknowledgment of the friendly greeting of his patient, Dr. Shelden was off to a good start when he called attention to an area of the patient's thorax and asked, "What do you see there?" We saw the patient breathe; we saw his heart beat; we saw a score of things, then carried away a lesson we never forgot: "It is a movement that you see, is it not?" That particular movement was a retraction of the chest wall caused by adhesive pericarditis. Nor did we forget the morning we spent with him simply in feeling pulses. The art of physical examination was at its best, and all that he could catch in the dragnet of the five senses left us spellbound and speechless. It was his slip of paper that lay on the autopsy table with the correct diagnosis, "Carcinoma of the stomach and congenital coarctation of the isthmus of the aorta," and his was the first diagnosis of pituitary tumor made in Minneapolis. Although thirty-five years have come and gone since then, his pupils at the University of Minnesota recall his clinics as though they had been held but yesterday, for in every master there is a touch of eternity.

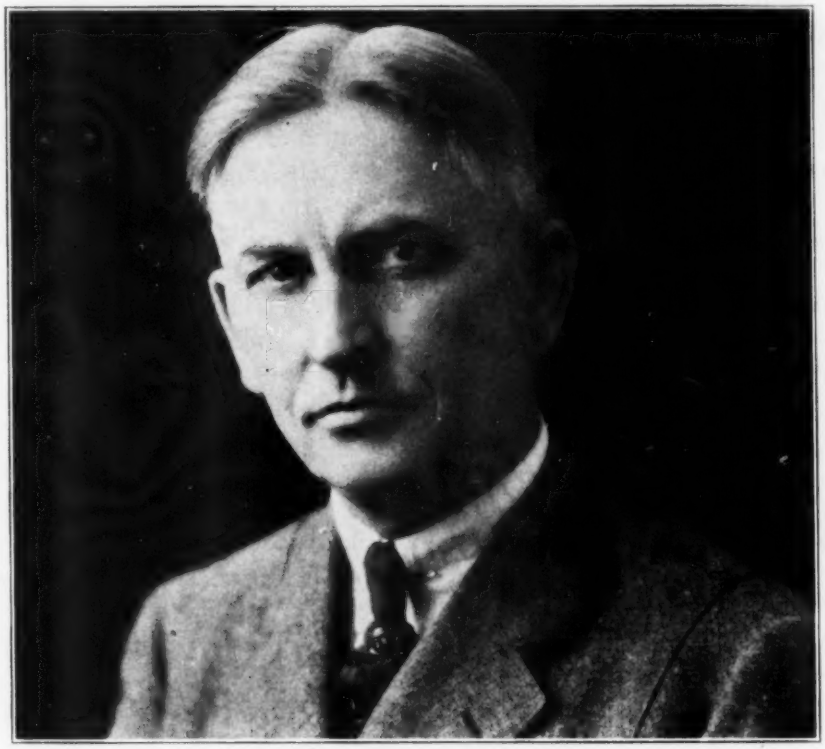
"Sometimes," he said, "it's wrong to be right," and he never hesitated to admit that he did not know. Reflexes were never "completely absent," for what could be more absent than "absent"? He seldom carried a watch, and since his day began at the City Hospital it often ended there. His patients would leave his office and wait for him next day, perhaps not too patiently, but ready to forgive. Mrs. Plumpandfussy, with a private elevator in her house and a retinue of physicians, left him unruffled. "Sit down," he would say, "what do you want?" "I want to get well." "Why do you want to get well?"

His examinations were pursued with cool and infinite patience. Little wonder that he turned to neurology, where his gifts could find expression and application. In 1913, he accepted the invitation of the Mayo Clinic to establish a section on neurology, and, at the same time, he was appointed professor of neurology, Mayo Foundation, Graduate School, University of Minnesota.

Fifty years ago, extended training for the profession of medicine was not mandatory. Walter Shelden prepared himself thoroughly for his life's work. He entered medical school in possession of the degree of

bachelor of science, which he had been granted by the University of Wisconsin. In 1895, he received the degree of Doctor of Medicine from Rush Medical College. He served as an intern at Cook County Hospital, Chicago, for two years, and finally he spent two additional years in graduate training in Vienna.

He was a courageous leader and was not impressed by undeserved criticism. His ideas were orderly and well formulated, and he was never caught speaking *ore rotundo* or "on stilts." He resisted publication of any article that contributed nothing new or that was no improvement on what already had been said well. His undisputed standing as an internist, his penetrating knowledge of clinical neurology and his unpretentious and genial manner left an indelible yet tender memory in the minds and hearts of hundreds of graduate students whose good fortune had taken them through his door. He administered his section in the Mayo Clinic on the theory that the less you belabor a hoop, the more smoothly it will roll.



WALTER DeWITT SHELDEN, M.D.
1870-1946

He was a member of the American Medical Association, the American Neurological Association, the American Psychiatric Association, the

Central Neuropsychiatric Association, the Minnesota Society of Neurology and Psychiatry, the Osler Medical Historical Society, the Alumni Association of the Mayo Foundation, Alpha Kappa Kappa, Alpha Omega Alpha and Sigma Xi.

Soon after I became his assistant, as we were walking home together, he spoke of things which made clear how close to his heart lay an abiding passion for justice, that true principle of humanity. Of progress and poverty, of philosophy and of religion, I was to hear much more. His numerous essays on these subjects were penetrating and subtle. Although written well, he could not be persuaded to have them published.

His deliberate movements and almost shambling gait led no casual observer to suspect a powerful physique capable of swift, smooth and well coordinated movement. As a student at the University of Wisconsin, he played on the baseball team, and he was also a member of the first football team of that university. Later, he took up golf, which he pursued with his usual thoroughness, expertness and good humor.

He was intolerant of the waste and destruction of natural resources that represented no effort of man to produce; and if he was immoderate in anything, it was in the affection he bore for a beautiful tree or a good piece of wood. The Country Club was his cathedral, and he helped build it with his own resources and with his own hands. On it, he planted thousands of trees, and now that he is gone it is becoming a monument of ever increasing beauty and value.

His admiration and respect for a good craftsman were profound, and he himself excelled in woodworking. His projects were planned with care; the execution of them was precise, and the product was always dignified, sturdy and lovely. His favorite wood was black walnut, and it must have loved him, too, since it responded to his efforts like a gem.

On the morning of Feb. 13, 1946, Dr. Shelden did not awaken from his sleep. His passing was just as he and we wished that it might be. Left to survive him are his wife and two sons, both of whom are physicians. His wish that his ashes might rest on the golf course, under the wide and starry skies and the trees he loved so well, has been respected. As Wordsworth thought of his own life, so those who worked with Dr. Shelden feel, "That there hath passed away a glory from the earth."

HENRY W. WOLTMAN, M.D.

## NIKOLAI NILOVICH BURDENKO, M.D.

### 1881-1946

In 1939, when Germany marched on Poland and the dreadful news of war echoed around the world, Nikolai Nilovich Burdenko was on his way out of the U.S.S.R. with Mrs. Burdenko to visit the neurosurgical clinics of the United States. Bitterly disappointed, they returned to Moscow.

In 1943, when the German armies had been held 50 miles from the gates of that capital, Lieutenant General Burdenko had become Chief Surgeon of the Red Army. The other posts which he held at that time bore witness to his amazing vitality and capacity for leadership: president of the National Research Council, president of the Association of Russian Physicians, director of the Institute of Neurosurgery, professor of Surgery in the First Medical Institute of Moscow, Stalin Prize winner, Academician and honorary fellow in the Royal College of Surgeons of England and in the American College of Surgeons.

Burdenko received his medical education in Tartu (Dorpat) where he shortly became professor of surgical therapy. From there he went to Voronezh as professor of surgery and finally to Moscow, in 1929. Here he organized the Institute of Neurosurgery. Beginning in a small way, the institute grew rapidly until, at the end of fourteen years, it housed 150 beds and ample laboratories.

In the assembly room of this institute there hung three full-length paintings, of Sklifassofsky, surgeon; Ivan Pavlov, physiologist, and Harvey Cushing, neurosurgeon. These three men may be considered his heroes in the profession, for he labored throughout his life to excel in surgery, in science and in his chosen specialty of neurosurgery.

His ambitions, however, were not alone for himself. He was an enthusiastic extrovert, who strove to stimulate the members of his own profession. In this effort he was eminently successful, for he gathered about him a school of brilliant pupils, who continued loyal to him. Among them are the surgeon Yudin; the neurosurgeon Koreisha; Sarkisov, neuropathologist and medical liaison officer in London, and Lebedenko, neurosurgeon and liaison officer in Washington, D. C. The distinguished neurologist, Professor Rappaport, was his friend and constant companion from their early days in Tartu, and he eventually took charge of neurology in the new institute.

Burdenko was a short, stocky, quick-moving man. He preserved his tireless energy and ability to work far into the night even in his later years, when deafness came upon him more and more completely. In 1942 a cerebral embolus deprived him of speech. However, he regained the ability to read and write almost at once and, nothing

daunted, continued to discharge his numerous duties by reading reports and writing out his orders.

Within the year he was able to speak again, although with difficulty; and, maintaining his leadership, he continued to demand exacting discipline among his juniors and received from them unfailing allegiance. Lieutenant General Smirnov, the youthful Chief of Medical Services in the Red Army, stated that, despite his disabilities, the surgeon in chief never ceased to serve his country and the medical services effectively.

Professor Burdenko must be considered the founder of neurosurgery in Russia and a principal organizer of medical research and teaching during the rapid expansion of medical education that preceded the war. Although fate prevented him for making personal contact with foreign neurologists and neurosurgeons of his day, a contact which would have helped him with technical detail, he nevertheless established in Moscow a modern institute and taught correct basic principles of surgery and neurology.

During a luncheon given for the British-American-Canadian surgical mission in Moscow in 1943, General Burdenko hurried momentarily from the room and wrote out a toast which he brought back to the interpreter. It was as follows: "I ask you to fill your glasses and listen to the few words I have to say: Our friendship must be closer; this is only the beginning of it. To our friendship in science, in life and in the world."

The heroic labor of this neurosurgeon has ended, while the world is seeking a way of peace. Let medical men in every land and with one accord respond to his farewell toast—"To our friendship in science, in life and in the world." And let this be "only the beginning of it"!

WILDER PENFIELD, M.D.

## CHRISTOPHER CHARLES BELING, M.D.
### 1873-1946

Dr. Christopher C. Beling was born in Colombo, Ceylon, on April 4, 1873, the son of a prominent lawyer of the colony. He was educated in private schools in Colombo and was graduated from Wesley College in 1891. In 1892 he entered the Ceylon Medical College and was graduated in 1897, having won a government prize.

For two years after his graduation he served in the government medical service as superintendent of the leper asylum and colonial surgeon of one of the provinces. He then went to Edinburgh for graduate work at the Royal College of Physicians and Surgeons there and was granted the degrees of L.R.C.P. and L.R.C.S. in 1900.

In June of that year he came to this country and was licensed to practice in New York state and started practice in New York city. As his interests were turning to neurology and psychiatry, he sought and obtained a position on the resident staff of the New Jersey State Hospital for the Insane at Greystone Park in 1901. There he served till 1907, when he entered private practice in Newark, N. J. This was his final move, for he remained in practice in Newark to the end.

Always he was interested in mental hygiene, and especially in boys. He founded the first juvenile clinic and bureau of mental hygiene in Newark, one of the first in the country, and was director of the bureau from 1919 to 1922. He was attending and consulting neurologist and psychiatrist to many hospitals in Newark and other parts of northern New Jersey.

Dr. Beling was a member of many medical organizations, including the Medical Society of New Jersey (judicial council, 1912-1946); the Morris County Medical Society (president, 1907), the New York Academy of Medicine, the New York Neurological Society and the New Jersey Neuropsychiatric Association (first president, 1933-1937). He was elected to membership in the American Psychiatric Association in 1904 and to the American Neurological Association in 1920.

Dr. Beling continued to be active in his practice until shortly before the end. In the summer of 1946 he went on his annual vacation to Mount Desert Island. He appeared well at this time, but in September cardiac decompensation set in, secondary to hypertension. He died quietly on Nov. 30, 1946. He is survived by his widow, a son, a daughter and a brother.

Dr. Beling was a gentle, modest sort of fellow. His interest in neurology and psychiatry was genuine and strong. Especially did he care for the psychiatric problems of youth, including delinquency, and he did much to arouse the interest of his community in these problems. Those of us who knew him best will miss him most.

LOUIS CASAMAJOR, M.D.

# News and Comment

## THE AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC.

The following diplomates were certified in December 1946:

*Psychiatry.*—By Examination: * John Alden, San Francisco; C. Knight Aldrich, Madison, Wis.; Adam G. Allen, Coatesville, Pa.; Herman S. Alpert, Marcy, N. Y.; Charles L. Anderson, Worthington, Ohio; Sam Beanstock, Downey, Ill.; Nathan Beckanstein, Brooklyn; Robert Eugene Bennett, Trenton, N. J.; John A. Bianchi, Brooklyn; Viola Bernard, New York; Margaret V. Beyer, Sykesville, Md.; Albert J. Boner, Madison, Wis.; Ina Helene Boyd, San Antonio, Texas; George Clayton Branche, Tuskegee, Ala.; Norbert Bromberg, New York; Warren T. Brown, New Haven, Conn.; Charles Buckman, Queens Village, N. Y.; Samuel Burack, Chicago; Edward Morse Burn, Philadelphia; James A. Campbell, Thiells, N. Y.; Elmer E. Capellari, Pittsburgh; Vincent James Cassone, Danville, Pa.; Carmelo Chiarello, Brooklyn; Dominick F. Chirico, Brooklyn; John Chornyak, Chicago; William J. Clauser, Boston; Irwin Justus Cohen, New York; M. Michael Cohen, Brooklyn; Henry A. Davidson, Newark, N. J.; John Evan Davis, Trenton, N. J.; Vernam Terrell Davis Jr., Ellis Island, N. Y.; Amerigo Philip Dell Cort, Canandaigua, N. Y.; Edward E. DeLong, Lyons, N. J.; Victor William Eisenstein, New York; Harrison Force English, Trenton, N. J.; Harold Feldman, Rochester, N. Y.; Leon Ferber, Nashville, Tenn.; Howard B. Finkelhor, Pittsburgh; Ernest J. Fogel, Harrisburg, Pa.; Henry Morgenthau Fox, Boston; Jerome D. Frank, Washington, D. C.; Vincent L. Frankfurth, Northampton, Mass.; Joe Edward Freed, Columbia, S. C.; * Arnold P. Friedman, New York; James Bauer Funkhouser, Richmond, Va.; William Furst, Newark, N. J.; Wilbert M. Gansloser, St. Louis; Harry Gershman, Central Islip, N. Y.; Leonard Gilman, Washington, D. C.; Leon Ginsburg, Cedar Grove, N. J.; Stewart T. Ginsberg, Marion, Ind.; Bernard C. Glueck Jr., Ossining, N. Y.; Lionel Goitein, New York; Morton M. Golden, Brooklyn; Joseph L. Goldstein, Asheville, N. C.; Meyer E. Golob, New York; Samuel T. Gordy, Philadelphia; Louis N. Gould, Norwich, Conn.; Henry G. Grand New York; Saul Greizman, Torrance, Pa.; S. Cyrus Grossman, Detroit; Peter B. Hagopian, Hathorne, Mass.; Solomon M. Haimes, Philadelphia; Louis Halle, Chillicothe, Ohio; Irving D. Harris, Chicago; Richard Lamar Harris, Los Angeles; William B. Hawkins, Lyons, N. J.; Harry Hoffman, Plainfield, N. J.; Charlton Gilmore Holland, Charlottesville, Va.; Joseph J. Hornisher, Fort Sam Houston, Texas; Elmer Leaman Horst, Coatesville, Pa.; Imre E. Horvath, Hines, Ill.; Ira L. Howell, Alamosa, Colo.; Charles B. Huber, Roanoke, Va.; William J. Hutchins, New York; Herbert W. Hyatt, American Lake, Wash.; Evelyn P. Ivey, Morristown, N. J.; Abraham I. Jackman, Chicago; Jack Reynolds Jarvis, Towson, Md.; Chester Earle Johnson Jr., Tuscaloosa, Ala.; Erich Kaufmann, Rochester, N. Y.; Frank Alfred Kay, Birmingham, Ala.; Francis W. Kelly, Hartford, Conn.; Cyril J. C. Kennedy, Kings Park, N. Y.; Walter S. Kern, Orangeburg, N. Y.; Robert Palmer Knight, Topeka, Kan.; Louis J. Kowalski, Philadelphia; Frederick H. Kramer, Philadelphia; Leonard Charles Lang, Buffalo, N. Y.; Gerald O. Laxson, Meade, S. D.; Martin Lazar, Ogdensburg, N. Y.; Harry Leaffer, Springfield, Mo.; Ann Hankins Leaman, Philadelphia; Louis Levinstim, New York; Lawrence A. Levitin, San Francisco; Erwin Levy, New York; Thomas Anthony Loftus, McLean, Va.; William H. Longley Jr., Greystone Park,

N. J.; Capt. Thomas W. McDaniel Jr., (MC), U.S.N., Fort Worth, Texas; Ivan A. McGuire, Detroit; Harry L. MacKinnon, Dayton, Ohio; William K. McKnight, Philadelphia; Rudolph S. Matthews, Columbia, S. C.; Albert N. Mayers, New York; Frank Mercurio, Coatesville, Pa.; John Charles Mergener, Los Angeles; Joseph S. Miller, New York; Burness Evans Moore, New Haven, Conn.; James A. Mosco, St. Louis; Lieut. Comdr. Charles S. Mullin Jr., U. S. N., Great Lakes, Ill.; Lloyd J. Nelson, Queens Village, N. Y.; Jack G. Oatman, Greystone Park, N. J.; William E. Olson, San Francisco; Arpad Pauncz, Lyons, N. J.; Frank Pearcy, Dallas, Texas; Rosco E. Petrone, American Lake, Wash.; Hugh M. Pierce, Rochester, N. Y.; Edward N. Pleasants, Marlboro, N. J.; Hyman Pleasure, Central Islip, N. Y.; Leopold A. Potkonski, Philadelphia; James H. Rankin, Los Angeles; E. Louis Reder, Brooklyn; Herbert Spencer Ripley, New York; William Rosenbloom, Downey, Ill.; Charles Russman, Middletown, Conn.; Robert Bruce Sampliner, Van Nuys, Calif.; Nathaniel Sandler, Detroit; Arnold A. Schillinger, Northport, N. Y.; Herbert T. Schmale, Ann Arbor, Mich.; Clarence M. Schrier, Kalamazoo, Mich.; Lee Goodrich Sewall, Lyons, N. J.; Albert M. Sherman, Weehawken, N. J.; Stephen C. Sitter, Milwaukee; Kenneth K. Slaght, Rochester, N. Y.; Alan Percival Smith Jr., Tuskegee, Ala.; Theodore P. Sohler, Hartford, Conn.; Curtis G. Southard, Fort Worth, Texas; Sidney L. Tamarin, Brooklyn; George Tarjan, Peoria, Ill.; James Sidney Tarwater, Tuscaloosa, Ala.; Abraham Tauber, Pontiac, Mich.; Christopher F. Terrence, Brooklyn; Harvey J. Tompkins, Arlington, Va.; Seymour D. Vestermark, Fort Worth, Texas; B. Frank Vogel, New York; Charlotte Frisch Walker, Ann Arbor, Mich.; David Royal Wall, St. Louis; Maurice C. Wander, Kings Park, N. Y.; Merna Mary Warne, Greystone Park, N. J.; Robert W. Webb, Washington, D. C.; Frederic Samuel Weil, New York; Jerome L. Weinberger, Boston; Joseph Weinreb, Elmsford, N. Y.; Samuel A. Weiss, Teaneck, N. J.; Max Weissman, New York; Paul Weitz, Lyons, N. J.; William Winick, Coatesville, Pa.; Robert Andrew Wise, Rochester, N. Y.; David Graham Wright, Providence, R. I.; Israel Zeltzerman, Augusta, Maine.

*Psychiatry.*—On Record: George F. Asselin, Kankakee, Ill.; Marion Prentiss Bailey, Hines, Ill.; Victor H. Bean, Fort Lyon, Colo.; Carl A. L. Binger, New York; Smiley Blanton, New York; Parker G. Borden, Canandaigua, N. Y.; Harry H. Botts, Marion, Ind.; Walter Garfiels Bowers, Reading, Pa.; Thomas P. Brennan, White Plains, N. Y.; Robert Homer Bryant, Alexandria, La.; Charles Henry Burdick, Minneapolis; Walter Painter Burrier, Bedford, Mass.; Joy Ricketts Carriel, Elgin, Ill.; Olin B. Chamberlain, Charleston, S. C.; Marcus A. Curry, Greystone Park, N. J.; Howard Crosby Curtis, Wichita, Kan.; Charles F. Davis, St. Cloud, Minn.; William Drayton Jr., Philadelphia; Raymond C. Fagley, Newark, N. J.; John Blaize Ferran Jr., Binghamton, N. Y.; Floyd K. Foley, Lexington, Ky.; Joseph C. Fulmer, Coatesville, Pa.; William A. Gardner, Togus, Maine; James Alfred Gould, Denver; Thomas W. Hagerty, Camarillo, Calif.; Hans Hansen, Canandaigua, N. Y.; Clifford E. Harkey, North Little Rock, Ark.; John LeRoy Haskins, Portland, Ore.; Carl Johan Hedin, Bangor, Maine; Roger P. Hentz, Fort Custer, Mich.; Hiram G. Hubbell, Newark, N. J.; James Richard Hunter, Kankakee, Ill.; Kristine B. Johnstone, Imola, Calif.; Avonia Eads Kiser, Imola, Calif.; David Lionel Liberman, Wood, Wis.; Louis V. Lopez, Fort Lyon, Colo.; William F. Lorenz, Madison, Wis.; Floy E. Lyon, Terrell, Texas; Harriet S. McCarthy, Kankakee, Ill.; Frank S. Marnell, Santa Cruz, Calif.; Cecelia K. Morris, Cleveland; Arthur Harold Mountford, Sheridan, Wyo.; George William Morrow, Kankakee, Ill.; John Francis O'Brien, Bedford, Mass.; Alfred S. Oliver,

Imola, Calif.; James C. O'Neil, Burlington, Vt.; Victor Parkin, Los Angeles; William L Patterson, Fergus Falls, Minn.; Guy Payne, Cedar Grove, N. J.; James Kenneth Pettit, Pass-a-Grille Beach, Fla.; James Stuart Plant, Newark, N. J.; Darley Garfield Plumb, Fort Lyon, Colo.; John A. Pringle, St. Cloud, Minn.; Margaret Antoinette Ribble, New York; William J. Riley, Indianapolis; Albert L. Roberts, Tuscaloosa, Ala.; Paul A. Royal, Lincoln, Neb.; Harry Rubin, Waco, Texas; Gettis Troy Sheffield, Gulfport, Miss.; Cecil B. Shrout, Chillicothe, Ohio; Dennis E. Singleton, Mendota, Wis.; Earl H. Snavely, Newark, N. J.; Arthur E. Soper, Kings Park, N. Y.; Edgar A. Stewart, Dayton, Ohio; John James Thompson, Danville, Ill.; William James Thompson, Pass-a-Grille, Fla.; Leo R. Tighe, Augusta, Ga.; Roland E. Toms, Northport, N. Y.; Letcher Evans Trent, Mendota, Wis.; James F. Vavasour, Greens Farms, Conn.; Willard H. Veeder, Sonyea, N. Y.; Raymond Farnham Wafer, Canandaigua, N. Y.; Guy H. Williams, Macedonia, Ohio; Leo Clement Woods, Knoxville, Iowa; Frederick L. Wright, Wingdale, N. Y.; Roy Carl Young, Covington, La.; Charles LeRoy Zimmerman, Danville, Pa.

*Neurology.*—By Examination: *Abraham H. Ascher, Brooklyn; *L. D. Borough, New Albany, Ind.; J. Robert Campbell, Tampa, Fla.; *Lewis J. Fielding, Los Angeles; *William A. Florio, Washington, D. C.; *Werner Hamburger, Utica, N. Y.; Frederick H. Hesser, Durham, N. C.; Daniel Solomon Jaffe, Washington, D. C.; *Emmett B. Litteral, San Francisco; *Harry B. Luke, West Brentwood, N. Y.; Clark H. Millikan, Iowa City; Veronica O'Brien, Valhalla, N. Y.; Fred Terry Rogers, Dallas, Texas; Ira Stanley Ross, Newark, N. J.; Dave Burnard Ruskin, Caro, Mich.; George A. Schumacher, Hastings-on-Hudson, N. Y.; *Herman Shlionsky, Montclair, N. J.; Jonathan M. Williams, Chicago; Emil Guenther Winkler, Long Island City, N. Y.; *Samuel A. Zeritsky, Philadelphia.

*Neurology.*—On Record: Mervyn Heller Hirschfeld, San Francisco; Harry Lee Parker, Rochester, Minn.; Alexander Hamilton Williamson, Pass-a-Grille, Fla.

*Neurology and Psychiatry.*—By Examination: Nicholas A. Bercel, Beverly Hills, Calif.; Sidney Cohen, New York; Albert J. Crevello, Philadelphia; Herbert J. Darmstadter, Philadelphia; Herbert Jackson De Shon, Boston; Robert L. Garrard, Providence, R. I.; Wilfrid M. Gill, Cleveland; Robert G. Heath, New York; Bruce Lynn Kendall, New York; Lincoln Lebeaux, Bogota, N. J.; Albert J. Lubin San Francisco; Richard Sherman Lyman, Durham, N. C.; Theodore Meltzer, Brooklyn; Paul G. Myerson, Boston; Milton R. Sapirstein, New York; Morris Weinblatt, Toledo, Ohio; Avery D. Weisman, Boston; Hyman G. Weitzen, New York; Leon J. Whitsell, San Francisco.

*Neurology and Psychiatry.*—On Record: Glenn John Doolittle, Sonyea, N. Y.; Francis Argyle Ely, Des Moines, Iowa; Charles Englander, Newark, N. J.; Walter Arthur Jillson, San Francisco; Herman Josephy, Chicago; Pat Murphey, Little Rock, Ark.; Groves Blake Smith, Godfrey, Ill.; Henry Greene Smith, Cedar Grove, N. J.; Erwin W. Straus, Lexington, Ky.; Hillel Unterberg, St. Louis; Hans Wassing, Paterson, N. J.

## AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC.

The tentative dates and locations of the next examination for certification by the American Board of Psychiatry and Neurology, Inc., are May 16 and 17, 1947, in Philadelphia. Applications should be in the hands of the secretary, F. J. Braceland, M.D., 102 Second Avenue, S. W., Rochester, Minn., ninety days before the examination is scheduled. The last possible date for filing is March 1, 1947.

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*The asterisk denotes complementary certification.

## RESIDENCY IN NEUROPSYCHIATRY, SOUTHWESTERN MEDICAL FOUNDATION AND VETERANS ADMINISTRATION

The Southwestern Medical Foundation in cooperation with the Veterans Administration is offering a three year residency in neuropsychiatry. Two years of this is divided into eight month rotation periods between the Dallas area and the Veterans Administration hospitals at McKinney and Waco, Texas. The third year is elective, and investigative work is included. Approximately one-half the required time covers inpatient psychiatry. The other half is work in psychosomatic medicine and mental hygiene, including child guidance. The Dean's Committee consists of Dr. Guy Witt, Dr. P. C. Talkington and Dr. Don Morris, as secretary. For further information, write the secretary of the Dean's Subcommittee for Neuropsychiatry, Southwestern Medical College, 2211 Oak Lawn Avenue, Dallas 4, Texas.

## NEW YORK SOCIETY OF NEUROSURGERY

The New York Society of Neurosurgery was recently organized. The organization is an outgrowth of a group of New York neurosurgeons who have met informally at regular intervals since 1939. The present membership consists of twenty-four neurosurgeons who practice in the metropolitan area. Dr. J. Lawrence Pool, of 195 Fort Washington Avenue, New York, is president. Dr. Sidney W. Gross, of 8 East Eighty-Third Street, New York, is secretary.

## RESIDENCIES IN NEUROLOGY, VETERANS ADMINISTRATION

Two additional residency training programs in neurology for physicians in the Veterans Administration have been organized. The residencies, which will vary from one to three years, according to the physician's previous experience, are designed to prepare residents for certification in neurology by the American Board of Psychiatry and Neurology.

One training program will be conducted under the joint auspices of Boston University School of Medicine, Tufts College Medical School and Harvard Medical School. Residents will be stationed at the Veterans Administration Hospital at Framingham, Mass. (formerly the Army's Cushing General Hospital), which has special units for the study of epilepsy, aphasia, paraplegia and electroencephalography, and a complete diagnostic service in neurology. Applications should be sent to Dr. Harry C. Solomon, chairman, Dean's Subcommittee for Neuropsychiatry, Harvard Medical School, Boston.

The other training program will be conducted at Jefferson Medical College and Clinic, Philadelphia, under the auspices of the Dean's Committee of the Veterans Administration, Philadelphia. Dr. Bernard J. Alpers, professor of neurology at the Jefferson Medical College, will direct the program. Applications should be sent to Dr. Edward A. Strecker, chairman, Dean's Subcommittee for Neuropsychiatry, University of Pennsylvania School of Medicine, Philadelphia.

Other medical schools affiliated with the Veterans Administration for residency training in neurology where training programs are already under way are:

| Medical School | Veterans Administration Hospitals and Clinics | Applications Received by |
|---|---|---|
| Cornell University Medical College<br>Columbia University College of Physicians and Surgeons<br>Northwestern University Medical School | Bronx, N. Y. | Dean Willard C. Rappleye, 630 W. 168th Street, New York |
| University of Illinois College of Medicine | Hines, Ill. | Dr. Lewis J. Pollock, Northwestern University Medical School, Chicago |
| University of Minnesota Medical School | Minneapolis | Dean Harold S. Diehl, University of Minnesota Medical School, Minneapolis |

# Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

## Physiology and Biochemistry

EXPERIMENTAL NON-PARALYTIC POLIOMYELITIS: FREQUENCY, AND RANGE OF PATHOLOGICAL INVOLVEMENT. DAVID BODIAN and H. A. HOWE, Bull. Johns Hopkins Hosp. **76**:1 (Jan.) 1945.

Bodian and Howe inoculated 37 rhesus monkeys intracerebrally with material from pharyngeal swabs of patients with poliomyelitis. Nine of the animals became paralyzed, and 1 had a nonparalytic infection. Pathologic examination in all cases "showed typical infiltrative and neuronal lesions in the spinal cord, of moderate to severe intensity, and a characteristic distribution of lesions in the brain. The one case of non-paralytic infection showed a histopathological picture quite similar to that seen in the paralytic monkeys."

The occurrence of a nonparalytic infection in 1 of a total of 10 monkeys inoculated intracerebrally compares favorably with observations on monkeys inoculated intranasally with human and chimpanzee stools.

Histologic examination of the brains of 23 of the animals which did not become infected revealed scattered perivascular infiltrations in the pia mater in 16. These were interpreted as nonspecific reactions to the inoculation. Passage to 2 normal rhesus monkeys of a suspension of the cord of each of 7 of these animals gave a negative result.

The range of anatomic changes in monkeys with nonparalytic infections, as in those with paralytic infections, was wide. The distribution, within the limits imposed by resistant centers, varied from arrest of the pathologic process near the portal of entry to severe and extensive involvement of all susceptible centers in the brain and spinal cord. The authors suggest that this variability may be a factor in the degree of resistance to reinoculation. GUTTMAN, Philadelphia.

THE CHEMICAL DETERMINATION OF TOCOPHEROLS IN LIVER AND MUSCLE: TOCOPHEROL IN URINE AND FECES. L. R. HINES and H. A. MATTILL, J. Biol. Chem. **149**:549, 1943.

Only one systematic study of the distribution of tocopherol in animal tissues seems to have been made, and this was accomplished by laborious biologic assay. Although direct evidence on the role of tocopherol in cellular metabolism is thus far confined to its action in muscle, its presence in other tissues, whether as functional or as stored material, calls for a reliable chemical method of assay. When the technic of Devlin and Mattill for the determination of tocopherol in muscle was applied to liver tissue, its shortcomings became immediately obvious. This paper describes the modifications by which that method appears to have been improved and made adequate for use with liver, urine and feces. The tocopherol content of rat and rabbit liver tissue from animals receiving diets high in tocopherol, commercial laboratory chow and vitamin E–deficient diets averaged 42.3, 22.1 and 22.6 (rat) and 86.8, 9.2 and 9.4 mg. per kilogram, respectively. Muscle tissue of the same animals averaged 11.9, 7.5 and 4.8 and 28.1, 8 and 5.7 mg. per kilogram, respectively. No tocopherol was found in the urine of rats with a high tocopherol intake, nor was evidence obtained for the presence of tocopherylquinone in liver or muscle or its excretion in the urine, although considerable tocopherol was found in the feces under those conditions. Evidence was obtained indicating

that not all the tocopherol is removed from tissues by simple extraction with organic solvents. The possible significance of these observations is indicated.

PAGE, Cleveland.

ELECTROMYOGRAPHIC STUDIES IN POLIOMYELITIS. PAUL M. KOHN, EDWARD M. ZUCKER and JOHN A. TOOMEY, J. Nerv. & Ment. Dis. **102**:433 (Nov.) 1945.

Electromyographic studies of the muscles of victims of poliomyelitis have produced contradictory results. One group of investigators (Schwarz and Bouman, and Watkins, Brazier and Schwab) found evidence of spasticity in weakened and paretic muscles, as shown by a characteristic pattern of action currents, whereas Moldover found little or nothing to support the belief that spasm was present in either the paralyzed muscles or their antagonists. In view of these contradictory findings, Kohn, Zucker and Toomey tested with the electromyograph the muscles of 13 patients ranging in age from 7 to 33 years, 12 of whom had had acute attacks of poliomyelitis within eighty days of the examination. The muscles in question were tested at rest, when passively stretched and when voluntarily contracted. In general, potentials were recorded from the agonist and the antagonist muscle simultaneously, one or both of which showed clinical paresis. An analysis of the results indicated that most paretic or paralyzed muscles in cases of poliomyelitis do not show electromyographic evidence of spasm at rest. Only 20 per cent of the involved muscles tested showed continuous and sustained potential changes even when passively stretched. An interesting finding was evidence of disordered reciprocal innervation, as shown by the presence of potentials of unusually high amplitude in the antagonist muscles when the agonist (weak or paralyzed muscle) was actively contracted.

CHODOFF, Langley Field, Va.

STUDIES REGARDING GLUTAMINE AND AMMONIA IN THE CEREBROSPINAL FLUID OF PATIENTS WITH NERVOUS AND MENTAL DISEASES. MEYER M. HARRIS, J. Nerv. & Ment. Dis. **102**:466 (Nov.) 1945.

It has been shown that there is an increased amount of ammonia in the spinal fluid of patients in status epilepticus. According to Riebeling, this is due to the diffusion of ammonia into the spinal fluid from deamination of adenylic acid in the brain. Another possible source of ammonia in the spinal fluid is through spontaneous hydrolysis of glutamine.

A group of 50 patients with various nervous and mental diseases were studied to determine the levels of free ammonia and glutamine in the spinal fluid. The elevation in the levels of ammonia found by previous investigators was not confirmed, and the author believes that such findings are the result of a technical error caused by failure to take into account the decomposition of glutamine into glutamic acid and ammonia.

The level of glutamine in the spinal fluid was found to be within normal limits in cases of cretinism, oligophrenia phenylpyruvica and mongolism. Although the level of glutamine in the blood drops notably during insulin hypoglycemia, there is no change in the level in the spinal fluid.

CHODOFF, Langley Field, Va.

INFLUENCE OF GALVANIC STIMULATION ON MUSCLE ATROPHY RESULTING FROM DENERVATION. E. C. S. JACKSON and H. J. SEDDON, Brit. M. J. **2**:485 (Oct. 13) 1945.

Although it has been proved experimentally that the atrophy of denervated muscle can be prevented to some extent by regular electrical stimulation of the muscle, the conclusion that equally satisfactory results follow the clinical employment of galvanism did not seem warranted without further investigations. Accordingly, Jackson and Seddon undertook a study to estimate muscular wasting by a "comparatively simple and not very accurate method." They present "a short undocumented account" of their findings. The volume of the hand was

measured by a simple fluid displacement method in 164 cases of paralysis of the ulnar nerve, only 54 of which were selected for this report. In only half of these 54 cases was galvanic stimulation employed in treatment.

It was noted that the application of ninety stimuli daily for six days a week almost completely prevented wasting except during the first hundred days after denervation, when the treatment reduced the rate of wasting. The earlier treatment was started the better the results, because the beneficial effect of galvanism was most noticeable soon after denervation. Galvanism did not seem to increase muscle volume but, rather, prevented the inevitable decrease. Observations in individual cases strongly suggested that recovery was better in cases in which galvanism was employed than in the controls, but success depended on the frequency of treatment. There still remains to determine whether galvanism is equally effective in preventing wasting in large masses of muscle.

ECHOLS, New Orleans.

CHANGES IN HUMAN VOLUNTARY MUSCLE IN DENERVATION AND REINNERVATION. R. E. M. BOWDEN, Brit. M. J. **2**:487 (Oct. 13) 1945.

Bowden presents a study of the changes in human voluntary muscle during denervation and reinnervation from the standpoint of histology, electrical reactions, electromyography and treatment of paralyzed muscle. The structural changes which occur after denervation are described in detail; they are primarily those of atrophy, and not of degeneration. Up to one year after denervation a good degree of functional recovery may be expected. The degree of functional recovery is also dependent on the nature of the lesion in the nerve. In cases of complete division of the nerve surgical intervention is necessary for recovery. Associated with the structural change there are immediate loss of tone and voluntary and reflex action and a more gradual change in electrical excitability. Electromyographic studies showed that there was no recordable electrical activity in human muscle for about twelve to twenty-eight days after denervation. From twelve to twenty-eight days after denervation fibrillation occurs and persists as long as any contractile denervated fibers remain or until reinnervation is taking place. Surgical repair should be undertaken as soon as possible. Galvanic stimulation has been shown to retard muscular atrophy.

ECHOLS, New Orleans.

## Psychiatry and Psychopathology

ELECTROENCEPHALOGRAPHIC AND NEUROLOGICAL STUDIES OF HOMOSEXUALS. DANIEL SILVERMAN and WILLIAM R. ROSANOFF, J. Nerv. & Ment. Dis. **101**:311 (April) 1945.

Silverman and Rosanoff studied 55 cases of homosexuality from the point of view of variations in the central nervous system. The cases were selected from the population of the psychopathic unit of the Medical Center for Federal Prisoners, the criteria for selection being the habitual assumption of the female role in the homosexual act or a history of repeated homosexual acts in the free world. Investigative methods included electroencephalographic recording; use of social service records, with special attention to neuropathic heredity, birth injury and severe illness in the first year of life, and routine neurologic examinations. Evidences of neuropathic heredity, such as criminalism, psychoses, mental deficiency, convulsions and alcoholism, was found in 41.8 per cent of cases. In 70.9 per cent of the series there had been an illness or injury possibly affecting the nervous system. In 29.1 per cent of cases there were both positive histories and neurologic findings. The electroencephalograms were classed as abnormal in 50 per cent, as borderline in 23.6 per cent and as normal in 25.5 per cent of cases. The most prominent abnormality was a bilaterally synchronous 5 to 7 per second delta rhythm, originating from the anterior region of the head.

The authors briefly review the literature on the constitutional factors in homosexuality and suggest that homosexuality may be one manifestation of a nonspecific, familial neuropathic tendency.

CHODOFF, Langley Field, Va.

AN INTERPRETATION OF THE DIVERGENT OUTCOME OF SCHIZOPHRENIA IN IDENTICAL TWINS. SILVANO ARIETI, Psychiatric Quart. **18**:587 (Oct.) 1944.

Arieti describes the case of a pair of monozygotic female twins in whom schizophrenia developed. He considers that the symptoms presented by the patients were fundamentally similar. He suggsts that the hypochondriacal complaints presented by 1 patient and the somatic delusions of the other may have been "two different degrees or two different manifestations of the same fundamental psychic derangement." The difference is perhaps more important as a sign of the relative intensity of the mental conditions than as pointing to basic differences between them. The psychoneurotic (hypochondriacal) symptoms of the one patient were most prominent just prior to her recovery from her delusions of infidelity, i. e., when she was coming out of her psychosis. He suggests that the neurotic symptoms were part of the defense mechanism against schizophrenia. That patient recovered "(*a*) who was the more athletic and less asthenic, in agreement with the findings of Kallman and Barrera; (*b*) whose prepsychotic personality was definitely more extroverted; (*c*) who had always shown better ability to cope with the problems of life, and (*d*) whose symptomatology was somewhat atypical because of the presence of many 'psychoneurotic' symptoms." The patient had no specific treatment. Her sister was as deluded as ever after 63 insulin shock treatments and at the time of writing had not lost her delusions.

McCARTER, Boston.

CLINICAL ASPECTS OF DEPRESSION. EDOARDO WEISS, Psychoanalyt. Quart. **13**:445 (Oct.) 1944.

Weiss states that the division of depressive states into (1) symptomatic depressions, depressive states that are consciously due to some other neurotic condition, and (2) essential depressions, in which the depressive state is itself the immediate and chief reason for the complaint and is not secondary to another neurotic condition, is a distinction hard to maintain because in all cases of the latter type analysis reveals deep neurotic conditions which have produced the depressive state.

Essential depressions have in common the libido-economic factor of lack of interest in anything. Reduction of interest leads to inhibition of activity. Some patients feel greatly distressed by the lack of interest and inhibition of activity; in others all ego feeling seems to he numbed.

A patient with simple depression also may display this numb ego feeling. He may show a decrease in the intensity of his self experience; he is less awake, and the external world conveys to him a much less intense emotional meaning than it does to other persons. In general, his affective responses are weaker. This phenomenon has to be distinguished from a simple lack of interest, although it may lead to such a lack.

Very often simple depressions are complicated by a pessimistic attitude: despondency, the desire to die, pessimism and world weariness.

Depressive states are frequently due to some strong fixation to a love object, which, however, is rejected by the patient himself, so that a great amount of libido remains blocked and unavailable. From the libido-economic point of view this phenomenon can be described as follows: A great amount of libido remains unconsciously attached to the mother or to some other love object, or remains directed toward an unattainable goal. Because of some strong disillusionment, a frustrating waiting for some kind of gratification that never comes, the patient begins to devaluate the object or goal, as though he wanted to convince himself of its uselessness as a source of enjoyment. The whole fixated libido exhausts

itself in this lasting affective attitude of rejection of a love object or goal which cannot be relinquished. This produces the clinical picture of an essential depression—the patient shows no interest in anything.

The most manifold neurotic conflicts may be hidden behind the clinical picture of depression. The depressive state is largely due to a continuous process of rejection of some infantile love object or goal, chiefly as a defense measure against an unbearable state of frustration or anxiety. If the analyst interrupts the patient's rejection of the corresponding frustrating goal or object, then the depression may easily be substituted by another clinical picture—hysteria, compulsion neurosis, or even some psychotic disorder—the form depending on the nature of the "rejected situation" and on the development and constitution of the ego. Thus, a depression is often a defense measure against some more serious psychic disorder. From this it appears that one should be very cautious in the analytic approach in cases of depression.

Melancholia is the clearest example of a narcissistic neurosis. The patient's narcissism is injured in the most obvious way: he has more or less lost the faculty to love himself; indeed, he hates himself. When a person becomes aware of guilt or inferiority and then becomes depressed, he is not in the same state as when he is unable to love himself. His self love is merely frustrated. An object love may undergo frustration in an analogous manner if the love object fails to correspond to expectations. In the melancholic response to an equivalent injury the love object would be abandoned and/or hated. The characteristic feature of melancholia is loss of self love and the development of self hatred, due, in the clinical picture, to feelings of guilt and inferiority, regardless of the origin of such feelings. Self accusations may in some measure correspond to reality; they may contain at least some kernel of truth.

In analytic practice melancholic manifestations are found in every kind of neurosis, since many patients experience transitory melancholic states during the course of analytic treatment. The provocation for such reactions is often found in the patient's growing awareness of his own objectionable features. In melancholic episodes which are a reaction to the realization of those aspects of the personality which are antisocial, dishonest or egotistical, the patient's awareness of such traits (Jung would call them his "shadow") is exaggerated. He may feel that he is a despicable, an unworthy person. This state may not yet be a melancholic depression, but if he can no longer love himself then he manifests melancholic characteristics. The inability of the patient to reach an integration between his antisocial wishes and his moral standards causes an unevenness in his ego feeling (a tension); and since in these cases the self love depends on the attitude of the superego, the patient begins to hate himself. This, then, is a melancholic depression. If a patient does not succeed in properly controlling his antisocial drives, the analyst generally welcomes any feeling of uneasiness or depression with which he may react to the realization of his antisocial attitudes, and for a certain time he is left in a low-spirited or depressed mood. Such a depression may be justified and constitutes the normal mental incentive for the development of a controlling power, of learning how to deal with all sorts of instinctual situations. Thus, depression and feelings of guilt may have an objectively valid motivation. Only if the guilt reaction is exaggerated, or, especially, if the patient displays signs of melancholia (self hatred, lack of self love) does the analyst have to intervene. He, as a superego substitute, must convey to the patient the feeling that he does not reject him but accepts him as a whole, that is, with his bad features, while at the same time he attempts to show the patient his good points. He also tries to make clear to him that every person has some antisocial attitudes, that perfection does not exist.

In melancholia there is a persecuting and a persecuted introject. Both introjects are located in the patient himself, so that he persecutes himself or, more correctly, one ego aspect persecutes another ego aspect. The persecuted part, however, may not simply be an introject, because it may or may not have arisen exclusively from an identification with another object. In the manic phase the

"objectionable" introject (the passive one) is projected, while the ego completely assumes the active role of the superego because it no longer feels able to embrace the condemned attitudes. The dominating ego state is the superego state, while other, condemned ego states appear detached from the ego feeling and are projected onto other objects. By means of the aforementioned projection the patient succeeds, in the manic phase, in avoiding conscious mortification and conflict. But since this projection can be withdrawn, allowing such mortifications to become conscious, he is continually threatened by the possibility of melancholia. This is a structural splitting of the ego. The ego aspects are split into two parts, the one subjectively felt as the proper ego (the self) and the other projected. The ego cleavage occurs along the line of demarcation between "id ego" and "super-ego." In paranoia the ego does not cling strongly to the superego; and it is the persecuting introject (the superego), not the persecuted one, as in mania, which has been projected, with the result that the patient feels himself a target of persecution. Prior to this projection the ego was obviously "melancholic," a melancholic state, however, which is resolved in an opposite manner. Thus where the patient with paranoia succeeds in preserving his narcissistic position, the patient with melancholia fails. The more paranoid a personality, the fewer are its possibilities of melancholia.

A successful early analysis in which the dynamic factors explained in this paper are not neglected is the best preventive of a climacteric and presenile depression or melancholia, and also of criminality, when hormonal changes present the ego with too difficult a task of integration.

PEARSON, Philadelphia.

A FURTHER CASE OF PARANOID PSYCHOSIS SUCCESSFULLY TREATED BY ADRENALECTOMY. C. ALLEN and L. R. BROSTER, Brit. M. J. **1**:696 (May 19) 1945.

Allen and Broster report the case of adrenogenital virilism associated with paranoid psychosis in a woman aged 26 in which adrenalectomy was followed by recovery to normal. The patient had previously received electric shock therapy, psychotherapy, insulin therapy and progesterone, without success. This was the sixth case which the authors had seen in which adrenogenital virilism was combined with a psychosis and the fourth in which the psychosis was schizophrenic in nature. They suggest the possibility, although rare, of the occurrence of a syndrome of adrenogenital virilism combined with a paranoid psychosis, since these conditions are occasionally seen in the same patient.

ECHOLS, New Orleans.

PREFRONTAL LOBOTOMY. FEDERICO PASCUAL DEL RONCAL, Arch. méd. mex. **2**:493 (Sept.); 564 (Oct.) 1944.

The author reports his experiences with a series of 27 lobotomies in 21 patients: 4 with psychasthenia, 3 with paranoid schizophrenia, 7 with catatonic schizophrenia, 3 with hebephrenia, 1 with schizophrenia superimposed on mental deficiency, 2 with involutional melancholia, and 1 with a psychopathic state. The modified technic of Freeman and Watts was used. Local anesthesia was given, with good results, in more than half the cases. When the patient was very agitated, sodium penthotal was used. None of the patients on whom the operation was performed with local anesthesia exhibited any severe psychologic reaction to the procedure. There were no terror reactions, as reported by Fleming and McKissock. The operation was bilateral and was done in one sitting. The only serious complication was hemorrhage due to the cutting of the anterior cerebral artery in 1 case; death occurred four days after the operation. One patient died nineteen days after operation with septicemia and another four days after intervention with meningitis. In 2 patients there were probably incisions into the frontal horns, with mild fleeting meningeal reactions.

Confusion, torpidity and even somnolence usually followed the second incision. There seemed to be more definite improvement in patients who exhibited severe

mental changes immediately after intervention than in those who showed such changes several hours later. The mental changes usually lasted twenty-four to forty-eight hours, rarely up to a week. Absence of anxiety and agitation was usually noted soon after the initial postoperative confusion. One patient became manic after the operation. Irritability and affective incontinence were rarely seen. There was puerilism in 1 patient after operation. Mild elevation in temperature for twenty-four to seventy-two hours was noted. In a few cases the blood pressure fell during the operation but returned to normal immediately afterward. Headache was frequent but was readily controlled with analgesics. One patient vomited for a few hours. Urinary incontinence was noted in 70 per cent, usually for not more than a week, though in 1 patient it lasted for a month; 1 patient had fecal incontinence for two days. No neurologic signs were noted except in the patient already mentioned, who died as the result of a cerebral hemorrhage. One patient studied electroencephalographically showed delta waves in the frontal region nine days after the operation.

For a short time after intervention most of the patients were frank and talked freely, with little evidence of control. The author reports 1 case of marked sexual erethism; in another case a refined and educated woman told risqué jokes. In both cases the marked changes in behavior lasted only a few days. The most important psychologic sequel of frontal lobotomy was loss of initiative. Two lawyers in the series were able to return home but could not resume their professional activities. Laborers and domestics, on the other hand, were able to go back to work without any evident impairment of efficiency. The author disagrees with those investigators who claim there is no impairment of intelligence. While the lobotomized patient may be able to do as well in a Binet-Simon test as before the operation, there is evidence that the more highly complex intellectual processes, such as judgment, critical faculties and initiative, are affected. Rorschach studies on a few of the patients showed diminished ability to synthesize and a significant narrowing of interests.

The best results were noted with affective disorders. In schizophrenic patients, even those in whom trend reactions persisted, anxiety and agitation were diminished after the operation. Of 6 patients with anxiety in the foreground, 5 had complete clearing of the psychosis and the sixth died after the operation. Two schizophrenic patients had good remissions considering the seriousness of the disease. Three of the 7 catatonic patients had complete remissions; 3 improved, and 1 failed to improve. One of the hebephrenic patients died nineteen days after the operation, 1 was operated on a few times with good results, and 1 had a partial remission.

SAVITSKY, New York.

## Diseases of the Brain

ANAEROBIC INFECTION OF THE BRAIN. N. I. GRASHCHENKOV, Am. Rev. Soviet. Med. **3**:5 (Oct.) 1945.

Grashchenkov reports observations on 607 patients with penetrating wounds and 318 patients with nonpenetrating wounds of the skull. Of this number, 350 patients were under observation at front line clearing stations equipped for bacteriologic study. Cultures of material from the wound were made at operation and when dressings were changed. The wounds of the brain showed Clostridium perfringens in 24 per cent of cases, Clostridium oedematiens in 4 per cent, Clostridium sordellii in 5 per cent and Clostridium butyricum in 10 per cent. The corresponding figures for nonpenetrating wounds were 6.7, 2.5 and 0 per cent. The clinical picture in cases of nonpenetrating wounds was considerably milder, and granulations formed promptly even in cases in which pathogenic anaerobes were revealed. Apparently. anaerobes did not find favorable growth conditions in the scalp and disappeared rapidly without producing a reaction. Perforation of the dura mater, however, opened a path for anaerobic infection of the brain. The frequency of anaerobic infection of the lower extremities and that of the brain showed considerable correlation.

Pathogenic anaerobes were isolated from the wounds of 87 patients under observation, or of 14.3 per cent of the patients with penetrating wounds of the skull. These patients were divided into those with acute, progressive and chronic infection and, finally, asymptomatic patients with pathogenic anaerobes in the wounds.

The patients in subgroup 1, those with gas gangrene of the brain, presented the following signs: protrusion and disintegration of brain tissue with necrotic and serous discharge from the wound; sharp putrefactive odor of the wound, with appearance of gas bubbles and edema of the surrounding brain tissue; early meningitis, the cerebrospinal fluid being xanthochromic and containing 100 to 400 cells per cubic millimeter and a slight increase of protein; severe pressure headaches, apathy and prostration; an increase in pulse rate and a slight increase in temperature; leukocytosis (12,000 cells) with lymphopenia, and high erythrocyte sedimentation rate (30 to 50 mm. an hour).

Gas gangrene of the brain almost always ended fatally within nine days. Apathy and disturbance of consciousness were produced by toxemia. Cl. perfringens was the predominating organism in infections of this type. Specific anti-gas-gangrene serum neutralized the toxins in cases of gas gangrene of the brain, as well as of the extremities. Large doses temporarily reduced toxemia, decreased apathy and improved the patient's condition.

Sharp, throbbing headaches and a sense of intracranial pressure, particularly near the wound, were caused by the specific edema-producing gas-forming action of anaerobes. This symptom also pointed to the presence of diffuse mild meningitis. A weak Kernig sign and slight nuchal rigidity were also present. The spinal fluid flowed under slightly increased pressure. The neurologic symptoms depended on the localization of the trauma.

The appearance of the wound of the skull was characteristic. The tissues, including the brain, appeared dirty and the adjacent tissues of the scalp dark gray and occasionally necrotic. The brain was friable, and there was no distinct boundary between the involved and the healthy tissue. Granulations were entirely absent. Liquid putrefactive detritus, with streaks of pus and frequently with air bubbles and foul odor, escaped under considerable pressure after incision and drainage. In some cases pressure sores occurred from proximity of the wound to trophic centers and from severe edema and toxemia.

Postmortem examination showed gangrene of brain tissue at the site of the wound and acute edema of the involved hemisphere and, to a less degree, of the opposite one. There were also parenchymatous degeneration of the heart muscle, liver and kidneys and hyperplasia of the spleen. A diagnosis of gas gangrene of the brain can easily be made at autopsy without microscopic examination.

Pathologic changes in subacute and chronic forms failed to show such clearcut characteristics. The chronic form was marked by encapsulated abscesses containing pathogenic anaerobes. They ruptured into the lateral ventricle and resulted in pyocephalus and severe purulent meningitis, particularly at the base of the brain. Macroscopically, these abscesses did not differ from similar abscesses containing putrefactive aerobes and pyogenic cocci. The presence of mixed pathogenic microflora gave the abscesses a distinctive odor. The subacute form of anaerobic infection might produce the same changes in the internal organs as the acute form. Pathologic diagnosis of the subacute form in some cases presented no serious difficulty.

Cultures obtained from wounds of the brain and from the internal organs in cases of acute and subacute infection always showed the presence of pathogenic anaerobes, chiefly Cl. perfringens, frequently in association with putrefactive anaerobes. The presence of pathogenic anaerobes in the internal organs, particularly the heart, indicated anaerobic sepsis in the majority of the fatal cases.

The histopathologic picture of the three forms of anaerobic infection revealed specific features. In cases of acute gas gangrene of the brain there were necrotic changes in the cortical cells with karyopyknosis, karyorrhexis and karyolysis.

Some distintegration took place in the deeper layers. An enormous number of bacilli were noted in the region of the wound and also in the opposite hemisphere. The brain substance was filled with gas bubbles and resembled Swiss cheese. There was a mild reaction in the gray and white matter surrounding the necrotic areas. Only occasional round cells and disintegrating leukocytes were seen. Silver and gold stains showed a mild proliferative reaction and degenerative changes in almost all the cells. The brain tissue displayed weak reparative power and only a mild inflammatory reaction. Absence of the border defense led to rapid spread.

Histologic analysis of the area of the wound in 5 cases of subacute infection revealed necrosis with many partly disintegrated polymorphonuclear cells in the periphery. In this boundary zone a sluggish reaction of the histiocytes was observed, which appeared granular. This process spread into the brain by perivascular routes. The walls of the vessels were infiltrated with round cells, and perivascular infiltration consisted of polymorphonuclear cells, glial elements, a small number of histiocytes and large bacilli. Special stains showed disintegration of nerve cell processes and swelling of protoplasm and nuclei of the glial elements. Few astrocytes were encountered in the region of the wound and in the periphery; they were distorted with short, swollen processes and shrunken cell bodies.

In cases of chronic anaerobic infection of the brain histologic examination of the surrounding brain tissue showed pronounced edema and swelling, the tissue resembling a sponge. At the margin of the abscess and throughout the hemisphere numerous degenerating histiocytes and granular cells containing lipids were observed. The nerve cells around the wound and, to a lesser degree, throughout the cortex showed necrosis and neuronophagia, together with destructive changes in the nuclei and protoplasm. There was an enormous number of large, thick bacilli. The vascular plexus of the affected hemisphere contained many distorted histiocytes. With chronic exacerbations diffuse encephalitis occurred. The increased virulence of the pathogenic anaerobes contained in the cerebral abscess damaged the connective tissue. The disturbance of its barrier function led to destruction of the boundary zone and to spread of the inflammation. In such cases there were observed serous meningitis, damaged hepatic cells and proliferation of the spleen.

The most effective method of preventing anaerobic infection of the brain is early and adequate surgical treatment of the wound, followed by administration of polyvalent anti-gas-gangrene serum. The author is convinced that cleaning and surgical aid within the first forty-eight hours after injury and adequate neurosurgical care prevented acute anaerobic infection of the brain. Powdered sulfanilamide in the wound did not prevent its development. The experience of the author at a special clearing station behind the front lines showed that the administration of large doses of polyvalent anti-gas-gangrene serum is essential in all cases of severely lacerated penetrating wounds of the brain.

The method of treatment of such infections under combat conditions, whether in the front lines or at the base hospital, consists in (1) removal of pieces of clothing, soil and foreign bodies, such as missiles, fragments of bone and brain detritus, and (2) combating the intoxication which occurs as a result of the growth of the pathogenic anaerobes.

From personal experience, the author believes that there is no basis for considering all cases of such infections as hopeless. With intensive therapy the disease may be changed from an acute into a subacute or chronic form, with better chances for recovery.

Patients with so-called chronic infection, with encapsulation and subsequent formation of abscesses containing the pathogenic anaerobes, were treated in routine fashion. In the case of a closed wound the author recommends puncture and evacuation of the contents of the sac and irrigation with a solution of sulfanilamide by the method of Spasokukotski and Bakulev or as described by American authors. It was not found advisable to remove the abscess, as this released the

barrier and resulted in rapid spread of an acute specific anaerobic encephalitis and purulent meningitis. An attempt should be made to separate the wound and the drainage tracts from the surrounding brain tissue. When an abscess is treated by puncture, it is recommended that the abscess sac be irrigated with a solution containing specific bacteriophage. Drainage of the opened abscess is recommended when a fistula is present. When the abscess harbors pathogenic anaerobes, it is wise to use three or four doses of polyvalent anti-gas-gangrene serum at the slightest sign of toxemia.

The polyvalent anaerobic bacteriophage is made up of phages against Cl. perfringens, Cl. oedematiens, Cl. sordellii and Clostridium oedematis maligni.

When the clinical course is favorable, the gangrenous portion of the brain gradually becomes dry, forming a crust, which separates painlessly. After this the patient's health improves and healing progresses normally.

A subacute form of gas infection was observed at the frontline clearing hospitals and at base hospitals. This form had a course of thirty to sixty days and was characterized by (1) malaise, lasting one month or longer; (2) considerable prolapse of brain tissue; (3) foul-smelling discharge, containing detritus and bubbles of gas; (4) rapid pulse and variable temperature, and (5) frequently signs of meningitis. A fatal outcome was less frequent than in cases of the acute form and death rarely occurred within one month. Bacteriologic examination of the discharge revealed putrefactive anaerobes, with fewer pathogenic anaerobes, and putrefactive aerobes. The methods of treatment are the same as those for acute gas gangrene of the brain, with local applications and subcutaneous injections of specific anaerobic bacteriophages.

The chronic form of gas infection of the brain occurred in 4.7 per cent of cases—usually encountered in the evacuation hospitals at the base and at some distance behind the lines. The duration of the disease was three to four months. This form was observed most frequently in patients who did not receive surgical or other special treatment at the front line clearing hospitals. The wounds usually contained various putrefactive anaerobes and pathogenic anaerobes. Treatment depends on clinical indications and is confined mostly to surgical drainage of the abscess after early diagnosis. To clear up the abscess repeated roentgenologic studies and surgical intervention are required. Anti-gas-gangrene serum is employed when signs of anaerobic intoxication appear.

The accurate diagnosis of anaerobic infection of craniocerebral wounds is established on the basis of bacteriologic cultures from the discharge and from the blood when sepsis is suspected. Constant bacteriologic control is necessary in the treatment of anaerobic infection of the brain. GUTTMAN, Philadelphia.

HEPATOLENTICULAR DEGENERATION: REPORT OF TWO CASES WITH PREDOMINANTLY HEPATOGENIC SYMPTOMS, ONE ASSOCIATED WITH THE CRUVEILHIER-BAUMGARTEN SYNDROME. ERIC WOLLAEGER and HARLEY C. SHANDS, Arch. Int. Med. **75**:151 (March) 1945.

Wollaeger and Shands report observations on 2 cases of hepatolenticular degeneration (Wilson's disease). The patients both presented a rare type of hepatolenticular degeneration in which the hepatic lesion was symptomatically the more prominent. One patient showed advanced disease of the basal nuclei, the symptoms of which disappear largely under treatment with stramonium. He was able to walk. Wilson has mentioned the fluctuating character of neurologic symptoms, but the progressive nature is not usually stressed. The same patient then exhibited evidence of the rare Cruveilhier-Baumgarten syndrome (congenital cirrhosis of the liver), characterized by portal hypertension with evidence of a pronounced umbilical collateral circulation. There was a loud abdominal murmur or thrill. He was then treated for his hepatic condition and received no further treatment for his neurologic symptoms, which he no longer needed.

So far as the authors are aware, this is the first case in which the essential clinical features of hepatolenticular degeneration and of the CruveilhierBaumgarten syndrome have been observed.

GUTTMAN, Philadelphia.

HEMIBALLISMUS. HAROLD KELMAN, J. Nerv. & Ment. Dis. **101**:362 (April) 1944.

Hemiballismus was first ascribed to a lesion of the corpus Luysii by Jacob, who also stated that a cerebral component was not necessary for the appearance of the condition but that the red nucleus, substantia nigra and pyramidal tracts must be intact. The syndrome is characterized by violent, uncontrollable, purposeless, throwing (ballistic) movements of one upper extremity or of the upper half of the body. They appear suddenly in one upper extremity and then in the homolateral lower extremity. They are rhythmic and continuous, are not influenced by psychic disturbances but cease during sleep. Kelman reports 2 cases, both with autopsy. The first was that of a merchant seaman aged 66 who suddenly began to have attacks of typical left-sided hemiballismus, followed by the development of left spastic hemiplegia and death. Autopsy revealed destruction of the entire right cerebral hemisphere. The posterior hypothalamus and structures distal to it were intact except for an area of destruction in the subthalamic body. In this case, the fact that the attacks at times involved only the hand and at other times spread to the face and to the lower extremity is evidence of somatotopic localization in the corpus Luysii. The second patient, a seaman aged 56, was hospitalized because of the gradual development of athetoid movements of the right extremities. Later there were mental changes and the sudden onset of violent throwing movements of the right extremities. The condition became progressively worse, and he died eight months after the onset of symptoms. Autopsy revealed carcinoma of the lung with a metastasis in the region of the left corpus Luysii. The lesion was so placed as to affect the subthalamicotegmental fibers.

CHODOFF, Langley Field, Va.

NEUROLOGICAL COMPLICATIONS FOLLOWING THE USE OF TYPHOID VACCINE. W. G. PEACHER and R. C. L. ROBERTSON, J. Nerv. & Ment. Dis. **101**:515 (June) 1945.

Peacher and Robertson report 2 cases in which neurologic complication followed the use of typhoid vaccine. The first case was that of a 28 year old soldier who was treated with intravenous injections of typhoid vaccine for resistant gonorrheal urethritis. After the fifth injection he had a series of generalized convulsions, and the temperature rose to 109 F. The next day there was evidence of left hemiparesis, accompanied with intense suboccipital headaches, confusion and drowsiness. Because of a recent head injury, a subdural hematoma was considered. Craniotomy was done on the right side, and a large, soft, necrotic mass was observed subcortically, which on microscopic examination proved to be degenerative. The second case was that of a 41 year old soldier in whom weakness of the right shoulder developed one week after the subcutaneous administration of 0.5 cc. of a bacterial vaccine made from the typhoid and paratyphoid A and B bacilli prepared by the Army Medical College. Examination indicated the presence of involvement of the axillary, musculocutaneous and suprascapular nerves.

In a review of the literature of the neurologic complications of treatment with typhoid vaccine, the authors found reports of Landry's paralysis, polyneuritis, neuritis of individual peripheral nerves and encephalopathy. The complications have been explained on the basis of anaphylaxis; the presence of a neurotoxin or attenuated virus or an associated latent bacterial infection, and stimulation of foci of infection.

CHODOFF, Langley Field, Va.

CENTRAL NERVOUS SYSTEM IN ACUTE DISSEMINATE LUPUS ERYTHEMATOSUS. DAVID DALY, J. Nerv. & Ment. Dis. **102**:461 (Nov.) 1945.

Daly reviews the literature on complications of lupus erythematosus disseminatus referable to the central nervous system. Toxic delirium, psychotic

states, convulsions, visual disturbances and headache have all been reported. The few neuropathologic reports permit of no clearcut formulation of the changes in the nervous system. Two cases are reported. In the first case there were shifting neurologic signs including weakness of the lower part of the face, reflex changes and a questionable Babinski sign. In the second case confusion and disorientation, headaches and twitchings of the extremities characterized a stormy course, with a fatal termination after twelve weeks in the hospital. At autopsy, the pathologic picture was one of diffuse nonspecific encephalitis with extensive vascular changes and thrombosis. There were acute and chronic degenerative changes in the nerve parenchyma secondary to disturbances in the vascular supply.

CHODOFF, Langley Field, Va.

A FATALITY INCIDENCE IN ELECTROSHOCK TREATMENT. ALEXANDER GRALNICK, J. Nerv. & Ment. Dis. **102**:483 (Nov.) 1945.

Gralnick reviews the problem of cerebral changes associated with experimental electric shock. The results have been contradictory, with considerable variation in the neuropathologic findings, depending on whether cats, dogs or monkeys were used. Whether the changes observed in the brains of the animals at autopsy are due to the direct action of the current on the parenchyma or to the production of vascular spasm and hemorrhage by the electric current has not been definitely determined. What part the convulsion itself plays is likewise undecided. Alpers and Hughes reported the observation of extensive punctate hemorrhages in the brains of 2 persons who died after electric shock therapy, but a review of the other 12 reported fatalities failed to show any important neuropathologic changes which could be directly attributed to the treatment.

The case is reported of a man aged 60 who was subjected to two electric shock treatments for a condition diagnosed as involutional melancholia. The day following the second treatment left hemiplegia developed and he lapsed into coma and died. Autopsy revealed the presence of a large cerebral tumor in the frontal fossa and adherent to the under surface of both frontal lobes. Microscopic examination revealed that this was a meningeal fibroblastoma. In addition there were multiple, scattered and confluent hemorrhages, mostly of recent origin. Other vascular changes present corresponded to the stasis and prestasis phenomena of Pickford and were due to the altered hydrodynamics of the circulation of the blood secondary to the increased intracranial pressure. It was felt that the electric shock treatment might have directly or indirectly aggravated these effects.

Thus, in this case, as in all the other reported instances of fatality due to electric shock, there was a complicating factor of sufficient severity to blur the findings and cast doubt on their general significance. All deaths have occurred in patients who received an excessive amount of treatment, were elderly or had a complicating disease, cerebral or vascular. The evidence at hand indicates that in the human being no specific structural pathologic change is directly referable to electric shock treatment. When electric shock produces permanent damage, there is usually preexisting disease, or the patient is especially sensitive to shock treatment.

CHODOFF. Langley Field, Va.

ROENTGENOLOGIC AND PATHOLOGIC ASPECTS OF PULMONARY TUMORS PROBABLY ALVEOLAR IN ORIGIN. E. F. GEEVER, H. R. CARTER, K. T. NEUBUERGER and E. A. SCHMIDT, Radiology **44**:319 (April) 1945.

Geever, Carter, Neubuerger and Schmidt report 6 cases of pulmonary carcinoma, probably alveolar in origin, with autopsy. Two of the patients were under 45 years of age, 1 being a 17 year old girl and the other a man aged 39.

In 1 case the condition was complicated by torulosis of the central nervous system. The patient was a woman aged 53 who complained of blurred vision,

difficulty in speech, drowsiness and loss of weight. The positive findings were emaciation, causeless laughter and giggling, bilateral nystagmus and slight stiffness of the neck. Budding, doubly refractive, yeastlike organisms were observed repeatedly in the spinal fluid, and torula organisms (Cryptococci hominis) were isolated from an inoculated mouse and guinea pig. Small areas of increased density in both upper pulmonary fields led to a roentgenologic diagnosis of fungous infection. At autopsy, tumor foci, measuring 0.5 by 1.0 cm., were observed in the lungs and leptomeninges and scattered through the brain. Microscopically, these consisted of cuboidal, epithelial-like neoplastic cells, in a papillary, alveolar arrangement. No cryptococci could be demonstrated, and the diagnosis of torula meningitis was not confirmed.

In 3 of the remaining cases the tumor was also of the multiple nodular type, while in 2 cases it was of the diffuse infiltrative type. Microscopically, all the tumors were much like that in the first cases.

Roentgenologically, in only 1 case did the tumor have the appearance of a primary pulmonary carcinoma. In 2 cases the appearance suggested a metastatic malignant growth in the lung, while in the other 3 cases the structure simulated that of a low grade inflammatory reaction (tuberculous, fungous or nonspecific pneumonitis).

In 2 cases there were no metastases outside the chest, while only in the case of torulosis were cerebral metastases seen. Metastatic sites in the other 3 cases included the periaortic and peripancreatic nodes, the liver, the kidneys, the adrenals and the pancreas.

The authors classify the tumors described as alveolar cell carcinoma, arising probably in the alveolar epithelium of the lung. This classification is based on the microscopic picture and the absence of a point of origin in a bronchus. The extremely rare "multiple pulmonary adenomatosis" is apparently a benign neoplasm also arising from the alveolar pulmonary cells simultaneously at different points.

Other investigators, however, believe the alveolar carcinomas arise from a single focus in a smaller bronchus and then metastasize rapidly to other parts of the lung via the bronchi and lymphatics.

TEPLICK, Washington, D. C.

METHYL BROMIDE POISONING: EFFECTS ON THE NERVOUS SYSTEM. A. BARHAM CARTER, Brit. M. J. **1**:43 (Jan. 13) 1945.

Among the toxic effects of methyl bromide poisoning are those on the nervous system. From a review of the cases described in the literature, Carter found subacute or chronic effects in approximately half the cases. The neurologic signs are central and peripheral. The central effects are headache, transient diplopia, difficulty in accommodation, dimness of vision, dysarthria, generalized incoordination and vertigo. Thus, the optic nerve, oculomotor nerves, cerebellar connections and posterior columns, with occasional involvement of the higher centers, producing psychic disturbances, are the parts primarily affected. The peripheral effects, which appear to be the result of a toxic peripheral neuritis, consist in numbness, tingling, flaccid paresis and loss of reflexes; there are few sensory changes except for loss of vibratory sense. Treatment is symptomatic; rest in bed and removal from exposure to the gas are sufficient, although convalescence may require as long as a year.

ECHOLS, New Orleans.

CHRONIC INTRACEREBRAL HAEMATOMATA. G. F. ROWBOTHAM and A. G. OGILVIE, Brit. M. J. **1**:146 (Feb. 3) 1945.

Rowbotham and Ogilvie describe 2 cases in which a congenital supraclinoid aneurysm became attached to the brain tissue and ruptured intracerebrally to cause a chronic hematoma with resulting hemiplegia. It was thought that some factor other than surface compression was the cause of the hemiplegia. The

secondary rise in intracranial pressure was suggestive of recurrent bleeding, but lumbar puncture proved absence of bleeding into the general subarachnoid spaces. After subsidence of the acute stage of the hemorrhage, the region of the anterior end of the sylvian fissure, wherein lie the middle cerebral artery and its many branches, was explored. A large cyst was encountered at a depth of 2 cm. in the temporal lobe of the brain immediately below the sylvian fissure; its contents were evacuated. Complete recovery of function followed in both cases. The authors explain the sudden impairment of consciousness at the time of rupture of the aneurysm on the basis of a combination of cerebral shock and widespread arterial spasm. The paralysis proved to be due to pressure of the cyst on the middle cerebral artery. The secondary rise in pressure was the result of breakdown of the intracerebral blood clot.

ECHOLS, New Orleans.

## Peripheral and Cranial Nerves

BILATERAL ACOUSTIC NEURITIS. M. R. JOHNSON, Arch. Otolaryng. **40**:261 (Oct.) 1944.

Acoustic neuritis has many etiologic possibilities. A review of the literature revealed that infection, vitamin deficiency and the toxic effects of drugs have been designated as causes. The condition usually comes on suddenly. It produces tinnitus and deafness when the cochlear branch is affected; vertigo, disturbances of equilibrium, spontaneous nystagmus and vomiting when the vestibular branch is involved, and a combination of these symptoms when both branches are involved.

The author reports a case of bilateral acoustic neuritis in a white soldier aged 23. Two days prior to admission to the hospital, the patient perspired freely while performing an arduous task in the Army. Military exigencies precluded his leaving his post even though the weather suddenly became colder. After about two hours he began to complain of throbbing pain in the right ear, sore throat and some stiffness in the muscles of the neck. The following day there was impaired hearing in the right ear but no earache. On his admission to the hospital a diagnosis of acute follicular tonsillitis was made, and he was placed under sulfanilamide therapy until the throat showed decided improvement. Six days after admission to the hospital, he complained of right-sided earache, and eleven days after admission, of deafness in the right ear. Hearing tested with the spoken voice was 20/20 in the left ear and 2/20 in the right. Three weeks after admission, the patient could hear nothing with the right ear, and a roaring sensation had developed in the left ear. Medical, surgical, genitourinary and dental consultations revealed nothing of significance. There were no other neurologic signs. In the hope of removing a possible focus of infection, tonsillectomy was done, but the progress of the disease was not curtailed. Ten months after the onset the patient was completely deaf in both ears. No definite statement regarding the cause could be made.

RYAN, Philadelphia.

MÉNIÈRE'S DISEASE. RICHARD F. MOGAN and C. J. BAUMGARTNER, Arch. Otolaryng. **41**:113 (Feb.) 1945.

Ménière's disease is a chain of disturbances, sudden in onset, in otherwise healthy ears, causing nausea, vomiting, loss of equlibrium, nystagmus and total or partial loss of hearing. It is significant that the vestibular and cochlear functions are damaged simultaneously and that frequently the ears are affected at the same time. There are four possible causes of the disease: (1) excessively strong impulses passing along the sympathetic nerves due to pathologic changes in the sympathetic nervous system itself; (2) an excess of vasoconstrictor substances in the blood; (3) an excess of histamine or histamine-like metabolites in the local area, and (4) hypersensitivity of the local area to metabolites, allergens or hormones. The view that exaggerated vasospasm is due to a fault of the

central mechanism, and not to a peripheral lesion, as many think Ménière's disease to be, is strongly supported by postoperative observations. The authors, in discussing 1 of their cases of Ménière's disease in which the superior cervical ganglia were removed, comment on the definite pathologic changes noted in the ganglia.

Apparently, sympathectomy does not completely stabilize the blood flow but prevents maximal constriction or dilatation. The authors call attention to the fact that Ménière's syndrome may be caused by many agents but that the mechanism is the same regardless of the irritant. A vasodilation or a vasoconstriction due to excessive stimulation of either branch of the sympathetic nerve to the internal ear causes excessive responses, as in Raynaud's disease. The effect is either an immediate excessive filtration into the scala media or a secondary reaction, following a marked vasoconstriction.

RYAN, Philadelphia.

NEUROFIBROMA OF THE CAUDA EQUINA. RAPHAEL POMERANZ, Radiology **44**:588 (June) 1945.

A 23 year old soldier was admitted with a history of recurring backache for five years, each episode lasting two to three weeks. There were long intervals between attacks. The episodes consisted of burning pain in the lumbosacral region, radiating into the right scrotum and the anteromedial aspect of the right thigh, with occasional numbness and tingling in the lateral portion of the thigh. The pain was aggravated by coughing, sneezing, twisting and bending. Immediately preceding admission, he had a severe attack following exercise, which completely incapacitated him.

Examination revealed a rigid spine, with muscular spasm, weakness and atrophy of both lower extremities, more pronounced on the right. The Lasègue sign was positive bilaterally. No pathologic reflexes were obtained. The spinal fluid showed an increase in protein (4,500 mg. per hundred cubic centimeters). Roentgenograms, showed a narrowed disk between the twelfth dorsal and the first lumbar vertebra, with a small osteophyte on the right side of the twelfth dorsal vertebra. The interpediculate measurement of the first lumbar vertebra was increased, with noticeable flattening of the pedicles.

Myelographic study with Pantopaque (an iodized poppyseed oil, with special cohesive properties) showed obstruction to the cephalic flow of the oil at the midportion of the first lumbar vertebra. A concave defect at this point indicated the presence of a rounded tumor. The diagnosis was that of a small neoplasm of the cauda equina, at the level of the first lumbar vertebra, intradural and probably a neurofibroma.

At operation an encapsulated tumor was observed at the suspected level. It was attached to the dura on the right and measured 2.3 by 1.6 by 1.3 cm. Histologic examination proved that the tumor was a neurofibroma. The patient made a complete and uneventful recovery and has been free from symptoms for about three months.

TEPLICK, Washington, D. C.

POLYNEURITIS AFTER JUNGLE SORES. R. L. WARD and A. S. MASON, Brit. M. J. **2**:252 (Aug. 25) 1945.

Ward and Mason report their clinical observations in 21 cases of peripheral neuritis subsequent to multiple indolent ulcers ("jungle sores") which occurred during a campaign in the Burmese jungle. The first symptom was blurring of vision, which usually appeared about seven weeks after the onset of the ulcers; sensory symptoms appeared about three weeks later. In the severer forms there were progressive weakness of the extremities, spreading to involve the hips and shoulders; astereognosis, and ataxia. Paralysis of accommodation was an outstanding feature of the disease. Examination of the nervous system revealed the characteristic signs of polyneuritis. Ward and Mason believe that the jungle

sores were infected with diphtheria bacilli and that the polyneuritis was of diphtheritic origin. If this hypothesis is accepted, prophylactic immunization of troops engaged in future jungle operations will become advisable.

ECHOLS, New Orleans.

## Treatment, Neurosurgery

MENINGOCOCCIC MENINGITIS: REPORT ON 165 CASES. ANDREW H. MEYER, Ann. Int. Med. **22**:543 (April) 1945.

Meyer reports on the results of treatment of 165 patients who had meningococcic meningitis.

In 150 cases the etiologic agent was proved bacteriologically. The remaining 15 cases were included because purulent spinal fluid was demonstrated and they occurred during an epidemic period of meningococcic meningitis.

The mortality rate was 5.3 per cent for the entire group and was 4 per cent for the 150 proved cases. In analyzing the causes of death, it was found that death occurred in 6 of the 9 fatal cases in the first twenty-four hours of hospitalization, the clinical diagnosis in 2 of these being the Waterhouse-Friderichsen syndrome. One death resulted from undue delay in diagnosis, and only 2 deaths occurred after adequate treatment.

Sulfadiazine was the chief therapeutic agent employed, but it is felt that meningococcus antitoxin and repeated lumbar punctures to relieve increased intracranial pressure were valuable adjuncts in certain instances.

The following sequelae were encountered: relapse, with subsequent recovery; ulceration of massive areas of purpura, with recovery; quadriplegia and respiratory paralysis, which were successfully treated by means of a respirator and repeated lumbar punctures; ptosis of the right eye and unilateral atrophy of the optic nerve; purulent effusions into the knee joint in 2 cases, in both of which the fluid was sterile on culture and subsequently cleared without drainage; questionable hydrocephalus, in 2 infants; purulent pleural effusion, in 1 case, in which the material was sterile on culture and cleared without drainage, and hemiplegia, in the case of a 59 year old patient with hypertension, in whom thrombophlebitis of the deep veins of the calf had developed.

GUTTMAN, Philadelphia.

THE QUESTION OF ELECTROSHOCK THERAPY IN THE DEPRESSIONS. NATHAN SAVITSKY and SIDNEY TARACHOW, J. Nerv. & Ment. Dis. **101**:115 (Feb.) 1945.

Savitsky and Tarachow recommend that courses of electroshock treatment of the depressions be shortened. They have found that permanent curative results have been attained after only three to five shocks in some cases, while, on the other hand, psychotic episodes have apparently been exacerbated after prolonged courses of treatment.

In 12 cases, courses consisting of five or less treatments were given extramurally in the office of one of the authors. In these cases, the endogenous depressive syndrome was relatively pure, and there was relative freedom from paranoid, hypochondriacal or neurotic symptoms. Treatment was continued only until the patient was free from symptoms, and there was a strong tendency to complete remission as a result of treatment. The remissions have lasted for from five months to two years.

CHODOFF, Langley Field, Va.

SHOCK TREATMENT IN PSYCHOPATHIC PERSONALITY. HARRY F. DARLING, J. Nerv. & Ment. Dis. **101**:247 (Mar.) 1945.

Darling describes the results of electroshock treatment in 3 institutional cases of psychopathic personality. In the first case no improvement was noted but definite remissions were obtained in the other 2 and both patients were able to

make good extramural adjustments. The author feels that his results justify further use of electroshock treatment in cases of psychopathic personality.

CHODOFF, Langley Field, Va.

ELECTROCONVULSIVE THERAPY IN THE PRONE POSITION. FRED FELDMAN, SAMUEL SUSSELMAN and S. EUGENE BARRERA, J. Nerv. & Ment. Dis. **102**:496 (Nov.) 1945.

In the course of administering combined insulin and electrical shock treatment, there was encountered the problem of preventing the patient from aspirating, during the electrical convulsive treatment, the mucus and saliva which accumulate during the stages of coma of insulin therapy. It was found that placing the patient in the prone position prevented this aspiration and was otherwise entirely satisfactory. The patient is placed in the complete prone position in an ordinary hospital bed. The head is kept in alinement with the rest of the body, the nose and mouth pointing straight down toward the mattress. The patient is supported by three assistants, and no undue extension or flexion of the back is permitted. The method has been used in approximately 50 cases without the development of any serious complications.

CHODOFF, Langley Field, Va.

AMINOACETIC ACID (GLYCINE) IN THE TREATMENT OF DEPRESSION. MAX H. WEINBERG, J. Nerv. & Ment. Dis. **102**:601 (Dec.) 1945.

Inspired by the successful use of amino acids in the management of surgical patients with nutritional difficulties, Weinberg treated 19 patients with depression with aminoacetic acid in doses up to 6 Gm. per day, administered orally in the form of the elixir (wine).

Most of the patients with mild depression recovered or improved, but 2 patients with involutional melancholia failed to benefit from the treatment. The author believes that the results are sufficiently encouraging to warrant a further trial of aminoacetic acid in cases of the mild depressions in which treatment can be carried out extramurally.

The improvement resulting from treatment with aminoacetic acid is explained on the basis of the action of the drug in counteracting the loss of appetite, which results in a lowering of serum protein and consequent damage to nerve tissue, possibly on the basis of cerebral edema. In addition, it has been proved that the administration of amino acids not only restores the nitrogen balance but also acts as a stimulant in increasing the patient's appetite.

CHODOFF, Langley Field, Va.

USE OF BENZEDRINE SULPHATE BY PSYCHOPATHS. H. J. SHORVON, Brit. M. J. **2**:285 (Sept. 1) 1945.

Shorvon reports the case of a psychopathic patient aged 35 who had been taking an average daily dose of 125 to 150 mg. of amphetamine sulfate at periodic intervals of many months for approximately four years without apparent physical ill effects or addiction. Withdrawal of the drug during one month of hospitalization resulted only in restlessness, sleeplessness and increased hunger; the patient stated that he felt no craving for the drug during that time. Although amphetamine sulfate is considered to have a hypertensive effect, the patient's blood pressure was normal.

ECHOLS, New Orleans

# Society Transactions

## NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

**Joseph H. Globus, M.D., *President of the New York Neurological Society, Presiding***

***Joint Meeting, Feb. 12, 1946***

**Parenchymatous Cerebellar Degeneration: Report of Two Cases.** DR. H. HOUSTON MERRITT.

Two cases were presented to illustrate the symptomatology of parenchymatous cerebellar degeneration. This syndrome was first described by Rossi in 1907 and by Marie, Foix and Alajouanine in 1922. Cases of this disease are characterized by the development of cerebellar symptoms in middle-aged persons without any family history of cerebellar disease. In the majority of cases the cerebellar symptoms are most pronounced in the lower extremity. Pathologic examination reveals gross atrophy of the superior part of the vermis and the lateral part of the hemispheres. Microscopically, there is massive destruction of the Purkinje cells with preservation of the basket cells. The cause of the condition is unknown, but chronic alcoholism has been considered a factor in a number of cases. The disease is more common than would be inferred from the small number of cases which have been reported in the literature.

DISCUSSION

DR. S. PHILIP GOODHART: I should like to ask Dr. Merritt his opinion of the classifications of clinical syndromes based on structural changes in the cerebellum and its contiguous and associated centers; I refer to such designations as olivocerebellar, olivopontocerebellar, parenchymatous cerebellar degeneration and the aplasias and dysplasias. The attempt to ascribe definite pathologic changes and localization to certain clinical entities has always seemed to me unjustified, and autopsy observations by no means confirm the clinical picture. Does Dr. Merritt feel that his 2 cases permit exact anatomicopathologic localization? I believe that the designation "parenchymatous cerebellar degeneration" is in keeping with the clinical picture in these cases, but I should like to know his feeling as to the difficulties in classification so often attempted in clinical textbooks and reports. In other words, do clinical signs enable one to localize the lesion? I doubt it.

DR. LEO M. DAVIDOFF: The second patient originally consulted me because some one made a diagnosis of cerebellar tumor; it was obvious from the history and the absence of increased intracranial pressure that he did not have a tumor, and I think that the differential diagnosis in his case is not difficult.

DR. H. HOUSTON MERRITT: It is not possible to make an accurate anatomic diagnosis in cases of this disease. One can only speculate that the patient has the type of clinical entity which has been described as parenchymatous cerebellar cortical degeneration. The classification of the cerebellar syndromes is confused, and there is not time to discuss it here. In the cases in which there is no family history of cerebellar disease and the onset of typical symptoms is in middle life, one can feel fairly certain that they fall into the category of parenchymatous cerebellar degeneration.

**Ophthalmoplegic Migraine and a Theoretic Explanation of Its Production: Report of a Case.** DR. FOSTER KENNEDY.

A white man aged 63 complained chiefly of double vision. In his teens he was subject to bouts of scotomas and right-sided headaches, which gradually increased

in severity, accompanied with nausea. The headache would last for a day and end after vomiting. During adolescence the headaches occurred as frequently as once every month or two. Occasionally after headache the patient's right eyelid would droop and he would see double for a day or two. As he grew older, the headaches became somewhat less severe but were regularly accompanied with and followed by diplopia for increasingly longer periods, until they would last as long as a month. As the patient reached middle age, the headaches became mild and infrequent, occurring only every six or twelve months. However, the double vision became permanent but was made still worse by mild headache. Vision had diminished in the right eye.

Physical examination revealed a generally healthy elderly man. His right eye deviated far to the right. It could not be turned beyond the midline. Movement produced by the superior oblique muscle was also absent. The right pupil was larger than the left; it was irregular and did not react directly to light. The consensual light reflex was sluggish in the right eye, and the right pupil reacted only slightly in accommodation to near vision. The corneal reflex was present on both sides.

This case was presented as one of ophthalmoplegic migraine. The pathologic process producing this condition has never been satisfactorily defined. According to the theory of migraine which most closely explains the clinical happenings, the migraine is due to localized intracranial edema, probably on an allergic basis, the edema fluid accumulating most frequently and to the greatest extent in the areas within the skull best adapted by formation and the exercise of gravity to permit its accumulation in bulk. The angle made by the slope of the tentorium and the convexity of the meninges is ideal for this purpose, and accumulation of fluid in this position would account for the zeigoscopia through irritation of the angular gyrus and for the transient hemianopsia and, if on the appropriate side, the alexia and the mild hemiplegic signs, often only of a sensory character, so often produced in the course of migrainous attacks.

Compression of the pituitary body by a similar collection of fluid in the sella accounts for the transient abnormalities of function of the pituitary gland which also occur. Collection of fluid in the neighborhood of the sphenoidal ridge can compress the nerves passing through the fissure and so block their function. Severe compression in such a bone-surrounded area can produce such anatomic change as to abrogate function for a time.

It is quite usual to find the paralysis of ophthalmoplegic migraine lasting for several weeks, and even months. It is to be expected that if attacks producing compression of these nerves occur regularly and frequently throughout the greater part of a lifetime complete degeneration of these nerves would result from these repeated insults.

Edema of the facial nerve produces facial paralysis because the bony aqueduct of Fallopius does not permit free swelling of the nerve, so that physiologic, and in some cases anatomic, block takes place. The same process often occurs in the optic nerve by reason of its fibers being tightly bound by the vaginal sheath of the nerve. One repeatedly sees spinal nerve roots giving signs of irritation or depletion of function in toxic states if the intervertebral foramens through which they pass are reduced in size as a result, for instance, of osteoarthritis.

### DISCUSSION

DR. H. A. RILEY: My own view of ophthalmoplegic migraine is that it does not exist as an idiopathic form of migraine. In every instance in which attacks of ophthalmoplegic disturbances have occurred in association with headache and postmortem investigation has been carried out, there has always been noted some element of pathologic character which interfered with the function of the particular nerve involved, and not, as Dr. Kennedy suggests, a merely transient functional disturbance associated with stasis of fluid in the vicinity of the nerve itself. Most of the disturbances one finds associated with migraine in which permanent sequelae follow attacks of a reversible character, as in the ophthalmic form, in

which eventual hemianopsia takes place, almost always prove to be the result of the development of arteriosclerotic or other organic processes. In such instances the condition begins with a transient interference with some neural function, and then, as the patient grows older and the sclerosing processes continue, an organic change develops in the blood vessels which results in a permanent defect, such as hemianopsia. In these cases of ophthalmoplegia, as in the cases of facioplegia, the pathologic evidence accumulated has not provided a firm basis for the recognition of these two disorders as a part of the migraine syndrome. In all the recorded cases, this ophthalmoplegia with headache should be looked on as such, but not as constituting a separate form of migraine. It is generally recognized that practically all lesions of the oculomotor nerve are associated with pain and with concomitant headache. Headache is a common accompaniment of all types of ophthalmoplegia. This is quite a different matter from the periodically recurring, transient attack of migraine, in which the patient shows a definite predisposition and there is a hereditary loading from his ancestors. I did not hear enough of Dr. Kennedy's presentation to know whether his patient had a hereditary history of migraine, convulsions, petit mal attacks, psychomotor equivalents or any of the other deviations which are usually found in the antecedents of people with true migraine. I think that until definite evidence is adduced it is unwise to speak of an ophthalmoplegic type of migraine. One can speak of recurrent ophthalmoplegia with headache, but not ophthalmoplegic migraine.

DR. H. HOUSTON MERRITT: I have never had the opportunity of examining pathologically patients with so-called ophthalmoplegic migraine, but I agree with Dr. Riley, on the basis of evidence from the literature and from my experience, that patients with headaches and palsy of the third nerve usually have an organic lesion which would explain the paralysis.

DR. FOSTER KENNEDY: What kind of lesion?

DR. H. HOUSTON MERRITT: Aneurysm or tumor.

DR. FOSTER KENNEDY: Do you mean to say that this man has had an aneurysm since the age of 16?

DR. H. HOUSTON MERRITT: I do not know what this patient has, but it is likely that he has a fixed lesion to explain the palsy of the third nerve.

DR. FOSTER KENNEDY: The patient has a history of attacks which cannot be called anything else but migraine. He has had them since the age of 16, and he still has them at the age of 66. Do you contend that he has an aneurysm? Dr. Riley says he had arteriosclerosis at the beginning, when he was a child.

DR. H. A. RILEY: I did not say that.

DR. FOSTER KENNEDY: That is just talking around the subject, instead of on it. Here is a man who has had typical migraine since the age of 16. He had attacks every month, which lasted a day; he vomited; he saw double, and he went on seeing double after every attack until he finally had a paralysis. I do not know why one should not call it ophthalmoplegic migraine; Charcot did, and his opinion was good enough.

DR. JOSEPH H. GLOBUS: Why do you object to the diagnosis of aneurysm in this case? The fact that the patient has had attacks of headache since he was 16 is not entirely out of accord with such a possibility.

DR. FOSTER KENNEDY: A sensible man bases his life on probabilities, not possibilities. "Possibilities" are lawyers' words. It is most unlikely that this man has had an aneurysm all his life—and one leaking each month or so—he is in good health, and there is no sign of an aneurysm. As he has grown older, his periodic headaches have almost ceased; so I believe my theory of migraine is correct.

DR. JOSEPH H. GLOBUS: Suppose I say an aneurysm is probably present, since he manifests clinical evidence favoring an aneurysm?

DR. FOSTER KENNEDY: He is a permanent employee of Bellevue Hospital, and when he is ready to go to the throne of God, I will let you know.

**Progressive Nuclear Ophthalmoplegia, Possibly on the Basis of a Vitamin Deficiency: Report of a Case.** DR. SAMUEL KAUFMAN (by invitation).

A 12 year old Cuban boy had the presenting difficulty of severe ptosis of both eyelids. He had had no neuromuscular disability until the age of 9 years, when he began to have trouble in raising his right eyelid. A year later he was unable to open either eye fully. The ptosis on both sides has slowly become worse. He has had no loss of visual acuity and no diplopia. Rest and fatigue play no role. His jaw never fatigues while chewing.

After uncomplicated pertussis, at the age of 2 years, the boy became a feeding problem. He ate little else than milk and starches until the age of 9. With the onset of his present illness, vitamin supplements in large doses were added to his diet. Neostigmine was given by injection and by mouth. No medication has affected his ptosis in any way. He has remained strong and vigorous, although small for his age—54 inches (137 cm.) in height and 57 pounds (25.9 Kg.) in weight. There has been no similar difficulty in the family, nor have any relatives had other congenital or abiotrophic neuromuscular disabilities.

*Neurologic Status.*—The abnormal findings were limited to his eyes. The visual fields were normal. Visual acuity was 16/20 in each eye. There was no nystagmus. The fundi were normal. The margins of the disks were sharply outlined. The pupils were of normal size and were round, regular and brisk in response to light. There was ptosis on both sides. On gazing straight ahead, the right palpebral fissure measured 2 mm. and the left between 2 and 3 mm. On upward gaze, the right palpebral fissure widened to 3 mm. and the left to 4 mm. There was also limitation of movements of both eyes in all directions. On looking upward, the right eye moved 1 mm. and the left not at all, as compared with the normal excursion of 5 to 7 mm. On looking downward, both eyes moved 5 mm., the normal being accepted as 9 to 10 mm. On looking to the right, the right eye abducted 5 mm., while the left turned inward 2.5 mm. On looking to the left, the left eye turned outward 2 mm. and the right inward 1 mm. The normal for all these movements is 9 to 10 mm. On looking downward, there was a slight inward rotation of the left eye, indicating that the superior oblique was less damaged than the inferior rectus. He did not complain of diplopia, but one of the visual images was suppressed, as could be shown by the mechanical movement of one eyeball, which failed to produce double vision.

The eyes were in normal position. The orbicularis oculi muscle was slightly weak on both sides, the left being weaker than the right. The eyelids elevated normally on wrinkling the forehead.

*Laboratory Data.*—The blood counts and the blood chemistry were normal; there was no eosinophilia. Examination of the stool showed only Trichiuris. The reaction to tuberculin was negative. Cutaneous tests for parasites, including Echinococcus, parasites of the Tinea group, Schistosoma and Trichinella, gave negative results. Basal metabolism tests, roentgenologic studies and gastric analysis gave normal results, and the specific tests for syphilis were negative. The only abnormality in the spinal fluid was an increase in the total protein to 100 mg. per hundred cubic centimeters.

*Conclusion.*—The patient has a slowly progressive external ophthalmoplegia. His difficulty started three years ago with ptosis. Now he has weakness, of a variable degree, of all the external ocular muscles and of the orbicularis oculi.

The clinical picture in this case is an interesting one. The etiology and the pathoanatomy of the condition are not definitely known. Possibly the disease picture is the resultant of a congenital nuclear poverty. Possibly there is an independent or associated slowly progressing degeneration of the nuclei of the ocular muscles.

Jolliffe, Wortis and Fein (The Wernicke Syndrome, ARCH. NEUROL. & PSYCHIAT. **46**:569 [Oct.] 1941) have shown the relationship between thiamine deficiency and Wernicke's syndrome. Avitaminosis during the seven years preceding the onset of this patient's illness must be considered as a possible etiologic agent.

DISCUSSION

CAPT. ARTHUR ALEXANDER KNAPP (MC), U.S.N.R.: This case has been most interesting. For a number of years my associates and I have done research on groups of young animals in the department of pharmacology, Columbia University College of Physicians and Surgeons. We induced deficiencies in vitamins A, B and D in these several groups and had a group receiving a low caloric intake. In addition to these animals, we had controls at all times. We watched these animals carefully from the inception of the deficiencies to the time they died or were killed, over a period of many months, and in none of them were we able to elicit any signs of internal or external ophthalmoplegia. Clinically, the ophthalmologic picture does not appear to be based on a vitamin deficiency.

DR. H. HOUSTON MERRITT: I should like to ask whether there was a history of ptosis or ophthalmoplegia in this patient's family.

DR. SAMUEL KAUFMAN: There was none.

DR. KURT GOLDSTEIN, Boston: I have seen a number of such patients. Their condition was very similar to this boy's. It began with ptosis, and later paralysis of the external ocular muscles developed. The intrinsic ocular muscles were never affected. One of these boys whom I had the opportunity of observing for many years later acquired paresis of one arm. I thought that the condition was a slowly progressive degeneration of the motor system. One of the boys had congenital syphilis.

DR. FOSTER KENNEDY: I should like to draw attention to the similarity of this condition to Wernicke's syndrome occurring with long-continued alcoholism and deficiency of thiamine.

DR. WILLIAM H. EVERTS: I do not know how long one should assume that this type of deficiency must go on to produce the ocular paralysis. Dr. Kaufman spoke of the European starvation, and there are probably a number here who saw European starvation in the war. I cannot say much about that, for there were no deaths from starvation in the prisoners whom I saw, There was a mass experiment, however, a bitter one, among the American and other allied troops who were taken prisoners by the Japanese and who starved for several years and lost from 60 to 80 pounds (27.2 to 36.3 Kg.) in weight; they had multiple neuritis of a severe degree, with optic nerve atrophy and central scotomas of all grades but no ophthalmoplegia. I had occasion to see many American prisoners brought down from Japan and hospitalized on Saipan and Oaku. Later in Manila, when the Japanese began to come out of the hills (the American Navy had cut off all supplies from Luzon in the fall of 1944, and they had no more food coming in, so that they had this period during which their diet was greatly reduced, consisting in roots and a small amount of rice, and they lost a great deal of weight—the Japanese is a small man anyway, but he lost as much as 50 per cent of his weight) when, I say, they began to come out of the hills in May, June, July and August, we American doctors would see them right on the trains, patient after patient, until in three months we had 6,500 patients; we found that the incidence of beriberi and other vitamin deficiencies was very high in that group, along with other diseases, such as parasitic disorders, malaria and dysentery, but there was no ophthalmoplegia. I had occasion to examine many of these prisoners myself and I know that they did not show as much ophthalmic disease as did the American, British and Australian troops, who had been on a longer starvation diet when they were imprisoned in Korea and Japan. I do not know how long, therefore, one can starve a man or how long he must be on a vitamin-deficient diet before the central nervous system breaks down. Perhaps others have seen it, but it has been commented on many times that intrinsic degeneration of the central nervous system did not occur often. We did see a few cases, in which the disorder was of the combined system type, with peripheral neuritis and degeneration of the optic nerves, beginning most often with a central scotoma, or in the American troops more often with a tendency to night blindness, which was progressive. Often a careful examination of the

visual fields would reveal a scotoma, even when in some instances the patient was not aware of it. A great many of these men responded to multiple vitamin therapy.

DR. CHARLES A. MCKENDREE: One finding in Dr. Kaufman's case disturbs me a little; that is the protein content of the spinal fluid of 100 mg. per hundred cubic centimeters. I should like to ask how that can be correlated with a vitamin deficiency or with a progressive degenerative process.

DR. H. HOUSTON MERRITT: Was a basal metabolism test done?

DR. SAMUEL KAUFMAN: I shall start with Dr. Merritt's question. We made three determinations of the basal metabolic rate, and all gave normal values. The boy did have an increased total protein content of the spinal fluid; I could not explain that adequately myself. Just how much of an increase one would have with a degenerative process in a small area of the central nervous system is questionable.

With respect to avitaminosis in the Pacific area not producing ophthalmoplegia, I can only say that the present case cannot be proved to be one of avitaminosis. I present it as an interesting case. There is a difference between this boy and the Japanese who came out of the hills in Luzon. They were adults. This boy had had vitamin-deficient diet from the age of 2 to 9 years, when he first exhibited ptosis and when vitamin therapy was instituted. Just what the importance of that fact is I cannot state.

DR. WILLIAM H. EVERTS: The Japanese had their wives and small children there, and we had many such families in prisons, often in an extremely starved condition; I assure you that they did not have ophthalmoplegia, for we kept them under observation.

**Treatment of Spasmodic Torticollis: Report of Two Cases.** DR. TRACY J. PUTNAM and DR. ERNST HERZ (by invitation).

It is by now quite clear that spasmodic torticollis is a variety of dystonia, to be distinguished sharply from disturbances in control of the muscles of the neck of hysterical origin. Occasional encouraging results from psychotherapy and orthopedic measures are probably to be ascribed to remissions or to confusion with other types of torticollis. Systematic psychotherapy in able hands has yielded poor results in a large series of patients treated at the Neurological Institute of New York.

The most widely successful surgical treatment is Dandy's modification of Foerster's operation, which consists in intradural section of the anterior roots of the first to the third cervical spinal nerves and section of the accessory nerves in the neck. A common technical error in carrying out this procedure is to overlook the first nerve root, which is hidden under a slip of the odontoid process. Section of the accessory nerve within the skull seldom produces complete paralysis of the sternocleidomastoid muscle, and section of the nerve just below the mastoid often fails to do so.

In cases in which the Foerster-Dandy procedure fails to give adequate relief, further decrease in spasm may be produced by a modification of the Finney operation, namely, section of the posterior divisions of the cervical roots as they emerge from the foramens. In this manner, the majority of the affected muscles from the fourth to the seventh cervical dermatomes may be denervated, without loss of power of important muscles of the hypoglossal group and of the shoulder. If there is a dystonia affecting the muscles of the back or the extremities, this may often be improved by an anterior chordotomy.

By performing these operations in series, graded to fit the needs of the patient, the majority of sufferers from torticollis may be given sufficient relief to enable them to return to their occupations.

DISCUSSION

DR. LEO M. DAVIDOFF: I should like to ask why it would not be wiser to continue the laminectomy and cut the posterior roots within the spinal canal lower down, that is, from the fourth to the seventh servical, and avoid these bilateral and bloody operations.

DR. H. A. RILEY: I should like to ask whether Dr. Putnam cuts the first, second and third cervical roots intradurally, and also whether he cuts the spinal accessory nerve, from which is derived the further innervation of the sternocleidomastoid and trapezius muscles.

DR. TRACY J. PUTNAM: May I reply first to Dr. Riley's question? Section of the accessory nerve within the skull does not always paralyze the sternocleidomastoid and trapezius muscles, and I therefore often have to cut the accessory nerve in the neck, and sometimes also the posterior divisions of the fourth to the seventh cervical spinal nerves.

In reply to Dr. Davidoff's question, let me point out that the paraspinal operation accomplishes a section of posterior divisions, not of posterior roots. As far as I am aware, division of posterior roots is without effect on torticollis and other dystonias, and motor divisions must be sectioned. I hesitate to divide the complete roots, of course, because this would involve the brachial plexus, but the posterior divisions of the anterior and posterior roots outside the cord can be divided apparently with impunity and still leave very good function of the muscles of the neck.

**Factors Causing Mass Spasms After Transection in the Cord in Man: A Reexamination.** DR. JOHN E. SCARFF and DR. J. LAURENCE POOL (by invitation).

Clinical studies showed great variation in both the segmental and the mass reflex activity of the distal segments of the spinal cord after its transection in man. No relation appeared to exist between the level of the transection and the presence or absence of spasms; and in the cases of spasm there was no constant time interval between transection and the appearance of spasms.

These considerations made it appear that the occurrence of mass spasms following transection of the cord could not be satisfactorily explained solely on the basis of the "release" of the isolated segments from the influence of the brain.

Surgical observations revealed marked pathologic changes in and about the distal stump of the traumatically severed cord, which included, in addition to dense adhesions anchoring the stump to the dura, extensive degeneration and gliotic changes within the cord itself.

It was also shown that this portion of the cord at the site of injury had a lowered threshold for both mechanical and electrical stimuli and that nervous impulses induced within this region in response to stimuli were readily transmitted to the more distal segments by way of the dorsal columns. It was further shown that surgical procedures which alter the anatomic condition of the stump caused alteration of the reflex activity of the cord below that level, and, finally, that striking amelioration of spasms could be obtained by interrupting one of the main pathways for transmission of impulses from the stump to the lower segments.

These observations made it clear that factors operating on or within the isolated portion of the cord—especially at the level of the lesion—could play an important role in determining the occurrence, as well as the severity, of mass spasms.

The following "irritative mechanism" was accordingly suggested: Constant or oft repeated traction on the adherent stump of the distal segment, or the irritative effect of gliosis within the stump, could increase the irritability of this portion of the cord and lower its threshold for afferent stimuli. Efferent impulses arising in this hyperexcitable zone are then transmitted to the more distal segments, chiefly by the dorsal columns antidromically, and probably by the internuncial, or propriospinal, system also.

The authors fully recognized that "release" of the cord from the influence of the brain played a primary role in conditioning the isolated segments for the development of spasms. They felt, however, that the actual occurrence of spasms in any given case of transection of the cord was determined by factors operating on or within the distal isolated segments, chiefly at the site of the lesion, and primarily irritative in nature.

DISCUSSION

DR. FRED A. METTLER (by invitation): A presentation which has been as quiet as this is likely to be passed over without one's realizing its heretical implications. However, what we have listened to is almost a complete negation of the present view of spinal man. This opinion of the condition of spinal man has been almost entirely based on the views of Head and Riddoch, gained during World War I. The number of cases of verified transection of the spinal cord in man that have been available for study has been extremely small; Head and Riddoch had 5 cases, of which 3 would measure up to the standard of the cases presented tonight.

What is the present knowledge of the condition of spinal man? A condition of shock is expected to follow transection of the cord, and after this passes it is assumed (not stated by Riddoch, but it has since become the opinion) that the initial reflex to appear is the Babinski. This has been taught in the literature. I suppose you noticed that in none of the present cases did the hallux go up. There were up-going toes in 1 of the cases. It is also said that the deep reflexes return in time and that they subsequently become uniformly overactive. The term "overactive" is used in a general way, commonly without qualification as to the state of the threshold, the area of the reflexogenous zone or the amplitude, force or speed of maturation. In the cases presented, you perhaps again noticed the striking lack of overactivity of the tendon reflexes.

These circumstances might, perhaps, create an erroneous impression. If the whole group of available cases had been considered, it would have been found that in some cases the hallux went up, in some it went down and in some it did neither; that in some cases the tendon reflexes were overactive, as judged in terms of threshold (that is, the thresholds were lowered), and that in others the reflexes were almost impossible to obtain. In some of the cases, if the full data had been presented, you would have seen that there was a variation from side to side in the condition of the reflexes.

It is assumed that after the state of reflex activity is reestablished in spinal man the reflex spread begins to develop. For example, if the patellar tendon is tapped, adduction on the other side occurs, and abnormal reflexes, such as the *reflexe des allongeurs* of Marie and Foix (that curious reflex in which pressure over the loins results in extension of the legs), appear. The stage is now set for the mass response. It is supposed that the mass response is an inevitable characteristic of spinal man in this stage. Nevertheless, here are a number of cases in which it did not occur.

One now has to face this array of facts. The series of cases which has been presented here is more extensive than any previous series (and I doubt whether a similar one will again become available for a long time). In all cases the patients were in good condition; in all the condition was long established, and in all cases on which these conclusions were based the presence of the transection was verified. The pieces of tissue which had been removed from the cord were quite without any conducting strands. Many of the specimens I examined myself, and there was nothing in them that could have conducted any impulses. The transections existed before the operation. In this series of cases we are unable to establish any constant picture. It is obvious that if one were so naive as to construct a diagnosis on a particular reflex one would get into trouble in a series like this. In addition, the general picture is not one of certain and inevitable release so far as the reflexes are concerned, nor is it consistent with the idea that massive spasm always develops.

Why massive spasm develops and why it is absent in some cases is the burden of the speakers' argument. To me, some of the other aspects of the presentation are more interesting, but the features of massive spasm would, perhaps, be more interesting to most of those here. According to the speakers, the ultimate cause of massive spasm is pathologic change in the proximal end of the distal stump. Perhaps, in viewing the spinal patient, we neurologists have

been a little too facile in our thinking about massive spasms; one is likely to recall tracts which normally exist in an acutely transected cord. But the spasms which appear usually occur at a time when many of these tracts, and all the long descending ones, have degenerated. The tracts have been cut; the axons have completely disappeared. It is therefore quite impossible that the spasm could be mediated by tracts which are descending. Therefore the only systems which may be operative in bringing the segments of the cord into the complicated functional correlation seen in massive spasm are the autonomic and the propriospinal system and the ascending tracts. These are the three possibilities. The work which the speakers have done indicates fairly conclusively that, however this integrating mechanism may be set off, the posterior funiculi are the integrating conducting mechanism *par excellence,* though perhaps not necessarily the only one. Stimulation of the posterior funiculi does not require the assumption of antidromic conduction in the full sense of the phrase, because this mechanism is provided with motor collaterals; in other words, the fasciculus gracilis (the fasciculus cuneatus is present only at higher levels) is normally provided with collaterals which connect with the ventral motor cells, whereas many of the other ascending systems do not directly establish such connections. However, the recurrence of massive spasm after the posterior funiculi have been cut would seem to indicate that other systems are available.

I should like to bring this material to your attention not merely as an incidental paper, but as a presentation of material which has been obtained out of a difficult war just fought, and which cannot possibly become available in such a correlated manner in any other way. It is a terrible price to pay for scientific knowledge, and we are required to learn all we can from such material when it becomes available to us.

DR. TRACY J. PUTNAM: Just to clarify the point, I should like to ask Dr. Scarff and Dr. Pool whether they are quite sure that the delay in the development of mass reflexes and spasms was not due to infection, for example, of the bladder. I think there can be no doubt in seeing these patients that they are in good general condition, but it is somewhat difficult to judge the incidence of minor sepsis without a specific statement.

DR. SIDNEY BERMAN: I should like to ask the authors whether curare was used in the cases with massive flexor spasm, and, if so, what effect was noted.

DR. JOHN E. SCARFF: In reply to Dr. Putnam's question, I can only say that at the time we saw the patients they were all on tidal drainage, the urinary tract was clinically clean, and the temperature within normal range. It was a practice overseas to place these patients with spinal injuries on tidal drainage very soon after they were wounded, as far forward even as the evacuation hospitals, and to carry them back while still under that treatment to the Zone of the Interior. The incidence of serious urinary sepsis in cases of spinal injury was slight in the European theater, and during our observation these patients of ours did not suffer from it.

As to the use of curare, we have not given that a fair trial; we are not prepared to express any opinion. I think it may have great possibilities.

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## NEW YORK NEUROLOGICAL SOCIETY

**Joseph H. Globus, *President, Presiding***

***Regular Meeting, March 5, 1946***

**Brain Tumor: Report of Two Cases.** DR. BENNO SCHLESINGER (by invitation).

Two cases of brain tumor of surgically unfavorable type, yet with excellent postoperative results, were presented.

DISCUSSION

DR. E. D. FRIEDMAN: I shall confine my comments to the second case, which was observed in the neurologic service at Beth Israel Hospital.

The patient was first admitted in December 1939, with a history of tinnitus in the right ear of three years' duration, deafness in the right ear, and numbness of the right side of the face of one year's duration. The significant findings included nystagmus to the right, absence of the right corneal reflex, sensory disturbances on the right side of the face and impaired hearing on the right, with lateralization to the left in the Weber test. There were also a number of small nodules under the skin of the forearms, which had been present many years. Biopsy of one of the nodules showed a lipoma. The patient refused to undergo operation.

In November 1941 she was readmitted with similar complaints and objective findings. The fundi were normal, but examination revealed slight weakness of the right side of the face of peripheral type and an equivocal plantar response on the left. Spinal puncture revealed clear fluid, which was under an initial pressure of 150 mm. and had a total protein content of 150 mg. per hundred cubic centimeters. Other findings were without significance. Vestibular tests yielded normal responses on the left side and absence of responses on the right. Roentgenographic examination of the skull revealed an enlarged sella turcica, with thinning and rounding of the posterior clinoid processes. The petrous ridges were normal. The patient again refused to undergo operation and left the hospital, against advice.

She was readmitted on June 28, 1945, with the chief complaints of inability to walk, a tendency to fall to the right and deafness and tinnitus on the right. She was lethargic and not well oriented. She cooperated poorly and was incontinent of urine. The blood pressure readings were 180 systolic and 110 diastolic. The fundi were normal except for suspicious blurring of the left disk. The other findings were as previously enumerated. In addition, the abdominal reflexes were absent; the tendon reflexes were more active on the left side than on the right, and there were manifestations of cerebellar involvement on the right side. A Towne view of the skull now revealed thinning of the upper wall of the internal auditory meatus on the right side. Caloric tests showed absence of labyrinthine responses on the right and slight hypofunction of the vertical canals on the left. The patient was persuaded finally to accept surgical treatment. Dr. Schlesinger has already reported on his operative results.

I should like to emphasize the long history, dating back to 1936, and the absence of definite papilledema. This might be explained by the cystic nature of the lesion and by its growth backward, toward the cerebellum, rather than medially, toward the brain stem. Drainage of spinal fluid from the ventricles was therefore not interfered with. It is interesting to note that the protein of the spinal fluid was high from the beginning of her illness. This is a usual finding in cases of acoustic neuroma. It is also worth mentioning that the hypoactivity of the left labyrinth was probably an expression of pressure against the brain stem. This was not sufficient, however, to produce contrecoup phenomena, which are frequently observed in the late stages of these growths.

**Encephalomalacia of the Cerebellum and Temporosphenoid Lobe: Report of a Case.** DR. T. E. BAMFORD JR.

The patient, an Italian-born housewife aged 55, had had remarkably good health until the age of 51. In August 1945, she was admitted to the Lenox Hill Hospital, complaining of pain in the left occipital and posterior parietal areas. Movements of the neck caused pain in these areas, but no nuchal rigidity was present. It was felt by the surgeon that her problem was functional, and after discharge she was referred to a psychiatrist who spoke her native language. Following his recommendation, seven electric shocks were administered. Exactly forty-eight hours after each electric shock she was suddenly nauseated and vomited food eaten during the last twelve hours. She was drowsy; her gait and station were normal, but

she showed a slight drift of the left upper extremity. Nystagmus to the left was observed. Lumbar puncture showed normal pressure; the serologic reactions were negative, and the protein measured 168 mg. and the chlorides 635 mg., per hundred cubic centimeters. One week later, during which her condition improved, there developed hyperreflexia on the left side, nystagmus to either side and drifting of the extremities to the left. No choking of the disk was observed, but because of the signs of a lesion in the posterior fossa a ventriculographic examination was made. This showed that both lateral ventricles were slightly enlarged, the left more than the right. The spinal fluid pressure was normal; the protein content was 92 mg. per hundred cubic centimeters. Seven days later she began to vomit and became drowsy. A pneumoencephalogram suggested, by excess of air over the cortex, some degree of cerebral atrophy. The signs of left hemiparesis, drifting to the left and bilateral nystagmus continued, while a Babinski sign appeared on the right side. She continued to grow worse; so it was felt that exploration was indicated. The left posterior fossa revealed a cyst in the cerebellopontile angle about the size of a small seedless grape. The diagnosis was still not clear. The patient recovered to the extent of becoming mentally clear and sitting up to comb her hair. Three days later her temperature rose rapidly to 106 F. Exploration of the operative wound revealed no infection. She died in a few hours.

Postmortem examination showed a cystic area, 4 by 4 cm., in the right inferior cerebellar lobe and one of similar size in the right temporosphenoid lobe.

Microscopically, both cysts showed lymphocytes and monocytes, perivascular collars of lymphocytes and many phagocytes containing pigment. The cerebrum was somewhat swollen. Evidence of operation was present.

The case is presented for discussion of the difficulty in explaining contralateral cerebellar signs, the possibility of electric shock as a cause of the terminal condition and the obscurity of the clocklike vomiting following each electric shock.

### DISCUSSION

DR. T. K. DAVIS: Thirty years ago I think this case would have been presented as one of "pseudotumor." That shows that time flies and one's habits of thinking change. I do not want to talk about the many conditions which simulate cerebral tumor. Probably the condition that is most usually confused is thrombosing disease of the brain; the common type, in which a large vessel is thrombosed, leads to a sudden focal lesion, as is all too familiar, and it is usually easily diagnosed. The other type of cerebral thrombosis is diffuse, with slower onset, and only in a later stage does it become focal. With the acute focal thromboses headache is the prodromal symptom. With the diffuse type there is headache also, but in addition there are various hypochondriacal symptoms—changes in behavior and many features which simulate psychoneuroses. I believe that the symptoms which Dr. Bamford described as appearing in his patient in the early part of 1945, and even earlier, were the prodromal symptoms of that type of thrombosing disease.

By the time the patient reached the neurologic service, the picture had changed. She showed drifting of the left hand and some ataxia and then hemiplegia of the same side. The high protein level of the spinal fluid—168 mg. per hundred cubic centimeters on one occasion and over 90 mg. on another—and the xanthochromia were permitted to outweigh the absence of papilledema and the absence of helpful signs in air studies.

Autopsy showed the necrotic areas in the right temporal region and in the right side of the cerebellum. One wonders why only the drifting and the ataxia on the opposite side were evident. Why was the side of the body on which the cerebellar lesion was present so free of signs? The second question is easier to answer than the first, for it is known that half the cerebellum can be removed surgically, or be absent as a result of agenesis, with few if any signs, and also that a slowly developing lesion produces fewer signs. One can understand, therefore, why there were no cerebellar signs on the right side. Their absence on the left side probably rests on histopathologic changes which I am not in a position to demonstrate tonight.

Perhaps I should comment on whether this tumor developed as a result of injury induced by the electric shock therapy. I do not think it did, and I doubt whether any one here thinks so.

DR. J. H. GLOBUS: Was the encephalomalacia of the temporal lobe and cerebellum established as a sufficient cause of death?

DR. T. E. BAMFORD JR.: The pathologic report listed the encephalomalacia as the cause of death, and I shall not try to explain it. The real cause of death probably was the surgical maneuvering in eliminating the neoplasm.

**Traumatic Hematomyelia with Unusual Features.** DR. AARON BELL.

A slow-witted Negro aged 32 in 1940 received fifty-two weekly injections for syphilis, some in the arm and some in the hip. The circumstances which brought him under my care began on Nov. 5, 1945. All that day he had been lifting bags of feed onto a truck. Toward the end of the day, as he was getting off the truck, the left leg gave way. On the morning of the sixth he consulted Dr. Carl Granger, who found paralysis of the left lower extremity and had him admitted to the Huntington Hospital. On November 7 a lumbar puncture was performed; after this procedure the right lower extremity became weak, and retention in the bladder and bowel developed. He remained in the Huntington Hospital from November 6 to November 10. While he was in the hospital, a retention catheter was installed. The rectal temperature ranged from 99 to 101 F.

He was transferred to the neuropsychiatric service of Lenox Hill Hospital on November 10. His temperature on admission was 101 F., his pulse rate 85 and his respiratory rate 20. Blood pressure was 130 systolic and 76 diastolic. Results of general physical examination were not noteworthy except that they confirmed the appearance of sound strength and good nourishment. The neurologic examination showed flaccid paralysis of both lower extremities; absence of knee and ankle jerks, neutral plantar reflexes and absence of the lower abdominal reflexes, diminished vibratory perception below the left anterior superior spine and impaired joint-position sense in the toes of the left foot; a level at the sixth thoracic dermatome on the left and the tenth thoracic dermatome on the right below which pinprick and temperature were not identified, and normal tactile sensibility. There was retention of urine and feces. No tenderness over the spine was noted.

Roentgenographic examination of the thoracic and lumbar regions of the spine was reported to show a normal condition. A manometric puncture showed a free subarachnoid space and xanthochromic spinal fluid, with a white cell count of 60 and a red cell count of 655 per cubic millimeter, and a 3 plus reaction for globulin. The total protein measured 95 mg., the glucose 38 mg. and the chlorides 682 mg. per hundred cubic centimeters. Culture of the fluid was sterile. The Wassermann reaction was negative. The colloidal gold curve was 0000112220.

The Wassermann reaction of the blood was 2 plus with the alcoholic antigen and negative with the cholesterized antigen. The Kline reaction of the blood was 3 plus. The white blood cell count on admission was 9,900, with 7,470 polymorphonuclear leukocytes.

The patient was in the hospital from Nov. 10, 1945 to Jan. 11, 1946, a period of sixty-three days. Throughout this time he had a spiking septic fever, the temperature ranging from 104 or 105 to 100 or 101 F., the pulse rate from 90 to 120 and the respiratory rate from 20 to 30, except in a period in which the respiratory rate ran as high as 44 a minute and he had pneumonia. The fever did not respond to penicillin and sulfadiazine, given individually or together.

The white blood cell count ranged from 9,900 or 7,740, on his admission, to 28,000, with 88 per cent polymorphonuclear leukocytes, on November 24, and to 22,800, with 84 per cent polymorphonuclear leukocytes, on December 17. Cultures of blood taken on November 13 and 17 were sterile. A guinea pig inoculated with spinal fluid showed no evidence of tuberculosis.

Routine urinalyses showed a 1 to a 3 plus reaction for albumin, from 15 or 20 up to 30 or 70 pus cells per high power field and occasional red blood cells. A culture of the urine yielded Aerobacter aerogenes.

Five days after his admission incontinence of feces developed. Trophic sores appeared over the buttocks and the sacrum; these spread and persisted up to the time of his discharge.

Eight days after his admission the left knee became tender, hot and swollen, and 100 cc. of straw-colored, clear fluid was aspirated by the orthopedic surgeon. The fluid was sterile, and the Wassermann reaction was negative. After aspiration, the swelling of the knee subsided and did not recur.

Two weeks after his admission a consolidation of the base of the right lung developed, which responded to administration of penicillin and sulfadiazine. The sputum was positive for Diplococcus pneumoniae (101 per high power field) and Micrococcus catarrhalis (130 per high power field). The spiking temperature which he had had prior to the appearance of the pneumonia showed no perceptible change during the pneumonia. The respiration became more rapid.

The neurologic status had progressed in many ways, so that on December 4, twenty-four days after his admission, the neural status was as follows: The sensory level to pinprick and temperature was still at the sixth thoracic dermatome on the left side and the tenth thoracic dermatome on the right. Tactile sensibility, which had not been affected, was now lost over the left leg as far as the fourth lumbar dermatome and was diminished from the sixth thoracic to the fourth lumbar dermatome; tactile sense was also diminished on the right side below the tenth thoracic dermatome. Vibration sense was lost below the anterior superior spine bilaterally, and joint-position sense was lost below the ankles. The knee and ankle jerks were absent. The plantar reflexes were neutral; the abdominal reflexes were absent. The patient was incontinent of urine and feces. He had large decubitus sores over the sacrum and buttocks, which did not respond to treatment.

In trying to formulate the problem presented by this patient the following facts had to be harmonized: (*a*) a history of sudden onset during work; (*b*) a history of treatment for syphilis, with the Wassermann reaction of the blood still moderately positive; (*c*) a considerably higher sensory level on the left side than on the right; (*d*) a continuous septic fever, with a corresponding leukocytosis, and (*e*) a xanthochromic spinal fluid with an elevated total protein content and negative serologic reactions.

Syphilitic thrombosis, hematomyelia and epidural abscess were considered diagnostic possibilities. The septic fever favored the conception of walled off pus; but the absence of spontaneous pain, the disparity in the sensory levels and the absence of spinal tenderness seemed to argue against an epidural abscess. The septic fever was certainly against the possibility of syphilitic thrombosis or uncomplicated hematomyelia.

The final tentative diagnosis was traumatic hematomyelia complicated by cystitis and decubitus ulceration. The strength of this conception lay in its best agreeing with the neurologic findings, since there is no neural picture too bizarre for hematomyelia; its weakness consisted in the necessity of resorting to the cystitis, urethritis and decubitus ulcers to account for the fever.

To be certain that pus was not being overlooked in the epidural space, an operation was performed by Dr. Echlin, who encountered a fracture of the spinous process of the fourth thoracic vertebra near its base. With the evidence of the fracture, the only plausible diagnosis seemed to be traumatic hematomyelia of the spinal cord. The mechanism of the fracture is hidden, perhaps by an inadequate history.

### DISCUSSION

DR. FRANCIS A. ECHLIN: I shall not attempt to discuss this case in detail but will present my observations at operation.

Laminectomy was performed on Dec. 19, 1945, approximately six weeks after the onset of symptoms. It had been decided to explore the cord in the region of the fourth thoracic vertebra, which would correspond approximately to the upper limit of the sensory segmental level. This, it will be remembered, was at the sixth thoracic dermatome on the left side.

A report of my observations follows: With the patient prone on the operating table, the spinous processes of the first, second and third thoracic vertebrae were normally prominent. This was true also of the fifth, sixth and seventh thoracic vertebrae, but the spinous process of the fourth thoracic vertebra was not prominent like the others. Nor could it be properly felt on palpation, there being a slight depression at this level, rather than the normal prominence. As soon as the incision in the skin was made and the ligaments were divided, it was evident that there was a fracture of the spinous process of the fourth thoracic vertebra. The process was freely movable in all directions, and when the ligaments had been stripped from their attachments a complete fracture through the spinous process near its base was visible. A laminectomy was now carried out on the fourth and fifth vertebrae and on the lower half of the spine and laminas of the third thoracic vertebra. No evidence of fracture of the laminas was present, and there was no compression of the spinal cord at this level. There was no evidence of an inflammatory process in the epidural space.

When the dura was opened, the spinal cord beneath the lower portion of the lamina of the fourth vertebra and under the lamina of the fifth vertebra appeared slightly yellowish. Otherwise, the cord appeared within the normal limits. The arachnoid was transparent and was not opened. A small catheter was passed freely upward and downward in the subdural space for a distance of about six vertebrae. There was, therefore, no obstruction in the spinal canal.

After operation, I again questioned the patient concerning direct trauma, but he always denied having had any. It is apparent, however, that he must have had one. Whether the fracture coincided with the onset of probable hematomyelia I am unable to say. Certainly, the level of the fracture corresponded with his upper sensory level.

I should like to ask Dr. Stookey whether he has ever seen a case of hematomyelia in which surgical intervention was of therapeutic value. By this, I refer to the question of drainage of a possible fluid hematoma by incision or aspiration between the posterior columns.

Dr. Byron Stookey: When I saw this patient at the Lenox Hill Hospital, I thought he had had an abscess, probably an epidural one, and made that diagnosis. A number of points here are extremely difficult to correlate with the usual conception of traumatic hematomyelia. First, this patient got off a truck and noted that the left leg was weak; the following morning he had paralysis of the left leg, and it was not until twenty-four or thirty-six hours later that he had paralysis of the opposite extremity. Up to this time there had been no disturbance of bladder function. It seems to me that this slow progression of symptoms is hardly compatible with what I know of traumatic hematomyelia. I should have expected that symptoms would develop immediately and that disturbance of bladder function would occur at the beginning; yet none of these things occurred. Furthermore, at the time Dr. Bell saw him, the patient had a disturbance of vibratory sense, which progressed for a time. At Dr. Bell's examination three or four weeks later there had been progression, so that there were considerable loss of vibratory sense and disturbance of tactile sensation. It is unusual in my experience to find such progression in cases of hematomyelia. Furthermore, the patient had a spiking fever from the very beginning, while he was still in Huntington Hospital, and this continued throughout the course of his illness. It is difficult to explain the appearance of a spiking fever before he had been catheterized, or even for a few days after catheterization. During his illness a swelling of the left knee joint developed, and 100 cc. of yellow fluid was removed. I should not know how to account for that on the basis of hematomyelia; I think it could be explained by an osteomyelitis with secondary effusion into the joint. If there were osteomyelitis, however, one would expect further spread of the osteomyelitis and evidence of the osteomyelitic process in the roentgenogram, which has not yet appeared. The evidence to warrant the diagnosis of hematomyelia is the unexplained fracture. This is an undoubted finding, and I presume that on the basis of a fracture of a spinous process at its

base one must assume direct trauma; yet the patient was unaware of any accident. He had performed the work of unloading boxes which weighed 100 pounds (45 Kg.); but this was his occupation, so that one cannot explain the fracture on the basis of unusual muscular effort. Nor have I ever known fracture of a spinous process to occur as the result of muscular effort.

The most likely diagnosis is hematomyelia, though I still accept this with reservation because there are so many points which cannot be satisfactorily explained in accordance with my experience with traumatic hematomyelia. In a case of traumatic hematomyelia I should expect the symptoms to occur at the time of the accident, and they would then regress, rather than progress.

DR. T. K. DAVIS: I cannot add anything to Dr. Bell's presentation. Dr. Stookey has pointed out the difficulties involved in the diagnosis. The patient was admitted with what might be called neurologically a picture of syringomyelia. In view of the operative observations, I think one is compelled to consider hematomyelia the proper diagnosis.

DR. PETER G. DENKER: In view of the difficulties of diagnosis in this case, I should like to recall a similar case of a boy at Bellevue Hospital. Dr. Friedman and Dr. Bell may remember this patient, who presented the clinical picture of syringomyelia on a congenitally syphilitic basis, with positive reactions of the blood and the spinal fluid. Furthermore, and this is the interesting point of similarity, while he was in the ward, a large swelling developed at the elbow, which yielded a clear serous fluid on tapping. Roentgenograms revealed a typical trophic joint. In view of the positive history of syphilis in Dr. Bell's case, it may be that the picture of hematomyelia can best be explained on this basis. Though it is true that hematomyelia can give a bizarre clinical picture, it is likewise true that syphilis of the spinal cord also presents a multiplicity of forms and that syringomyelia on a syphilitic basis has been repeatedly described in the literature. Dr. Foster Kennedy and I reported the case of this boy (Congenital Syphilitic Syringomyelia with Arthropathy of the Elbow, *J. A. M. A.* **114**:408-409 [Feb. 3] 1940).

I should like to ask Dr. Bell whether his patient was given antisyphilitic treatment after the lesion of the spinal cord presented itself.

DR. AARON BELL: He had previously been given antisyphilitic treatment.

DR. RICHARD BRICKNER: I hoped that there might be some discussion of the slow development of symptoms of hematomyelia. I recall a case which was reported at one of the conferences on Dr. Riley's service at the Neurological Institute that appeared to be one of hematomyelia. In this case the symptoms appeared over a period of forty-eight hours. Since then I have seen a similar case. It may be that now and then in hematomyelia there are progressive edema and continued seepage of blood. I raise this question because I am unaware of any accepted explanation of the phenomenon. For that matter, I am not certain that these cases of slow development have been proved beyond doubt to be cases of hematomyelia. If any one has additional information on this matter, I should like to hear it.

DR. IRA COHEN: Perhaps I can answer Dr. Echlin's question in part by reference to 2 cases, in 1 of which there was a real, and in 1 a possible, history of trauma. In the first case, there was a history of trauma, although it had probably no relation to the hematomyelia. A schoolboy fell on the steps at school and was brought into the hospital. I am sorry I cannot recall the details of the progression of the clinical picture, but there was a well defined sensory level, at which I made an exploration. The appearance of the cord was unmistakable in that it was much enlarged and a blue-black hemorrhage was shining through. I incised the cord; there was temporary improvement, but only temporary, and not very much. As I recall, the patient ended his days in Montefiore Hospital, and the hematomyelic cavity was observed to extend from the upper thoracic down well into the lumbar region. While there was a history of trauma, the hematomyelia was probably not of traumatic origin.

The second case is rather more to the point in that an iceman was struck in the lower thoracic region with a large cake of ice with immediate onset of para-

plegia and signs of bladder involvement. Just above the conus a hematomyelia was seen, an unmistakable picture on the operating table, with blue-black hemorrhage showing through. There was improvement in motor power but not in bladder function.

**Value of Penicillin in Treatment of Neurosyphilis.** DR. BERNHARD DATTNER.

Proper evaluation of success in treatment of neurosyphilis has been a problem since Wagner-Jauregg, twenty-seven years ago, reported that malarial treatment of dementia paralytica had brought about satisfactory results in a considerable number of his patients. At that time there were no objective criteria to prove his point other than the clinical improvement which enabled the patient to regain his former social status. However, since temporary remissions were not uncommon in cases of dementia paralytica, many authorities wondered whether the disease process had been definitely arrested and asked for an extended period of observation. A few years later it became obvious that fever therapy, unlike any other form of treatment, prolonged the life span of the patient with this disease. It remained uncertain, however, whether or not the stationary clinical level would be permanently maintained. The closest clinical scrutiny failed to answer this question. It was learned that irreversible and reversible signs and symptoms exist side by side in the disease; that improvement of symptoms may be only transitory, and therefore misleading; that signs and symptoms may persist, or even become more pronounced, although the syphilitic process has been definitely arrested, and, finally, that the syphilitic infection may be very active within the central nervous system and still be asymptomatic.

In view of these difficulties, my colleagues and I turned our attention to the study of the changes in the spinal fluid accompanying the dementia paralytic process and its reversal. We instituted a parallel follow-up study of the clinical status of the patient with frequently repeated examinations of the spinal fluid and soon, as far back as 1923, became convinced that the proper evaluation of the spinal fluid syndrome would enable us to forecast with a considerable degree of accuracy the final outcome of the patient's clinical course. With due attention to all parts of the spinal fluid spectrum, we learned to differentiate between findings indicating the unabated progress of the syphilitic process and those representing the reversal and the final disappearance of the inflammatory degenerative reactions. We finally were able to establish some general rules pertinent to the management of neurosyphilis which, with rare exceptions, have been proved to be valid by most of the workers in the field.

Clinical manifestations are not always a reliable criterion of activity of the syphilitic process. The serologic reactions of the blood are also of little help. The spinal fluid syndrome gives the needed guidance provided the tests are carefully performed and rightly interpreted. The Wassermann test of the spinal fluid determines the specificity, but not the activity, of the process. The presence of more than 4 cells per cubic millimeter indicates activity. Increase of total protein may indicate activity, as may the colloidal gold curve. In cases in which treatment has been carried out, the Wassermann and colloidal gold reactions of the spinal fluid may continue positive for varying lengths of time after treatment has been successful in checking the syphilitic process. If the cell counts are normal and protein determinations show definite improvement six months after therapy is discontinued, it is most unlikely that the infectious process will again become active within the central nervous system. With the advent of penicillin and the demonstration of its remarkable efficacy in the treatment of systemic syphilis, it followed that penicillin would be used in the treatment of neurosyphilis. Again, the question arose how to evaluate the therapeutic effect of the drug, and it was generally felt that an observation period of many years would be necessary to come to a definite conclusion. We, however, having gone through the same difficulties twenty-five years ago, were confident that with the standards we had established the task would be an easier one than was assumed. We were anxious to see whether the follow-up studies of

the spinal fluid syndrome would duplicate all the data which had been observed during the era of fever therapy. Meanwhile, more refined tests, including the titration of Wassermann reagins, electrophotometric determination of the protein content of the spinal fluid and the quantitative determination of the colloidal gold reaction, have become available. All the observations we have so far made on our patients have reaffirmed our original concept that the tendency of the syphilitic process is reflected in the spinal fluid findings and can be read like a spectrum.

The six month interval between the termination of fever therapy and reexamination of the spinal fluid seems too short in the follow-up study of patients with neurosyphilis treated with penicillin. So far, we have observed a subsequent relapse in 3 patients who showed a satisfactory response to treatment as indicated by the spinal fluid syndrome at the end of six months. For this reason, it seems advisable to assume a somewhat reserved attitude toward the transitional spinal fluid spectrum if it is to be evaluated before one year has elapsed.

We have treated a few patients who failed to respond to 2,000,000 units of penicillin with larger doses and have obtained satisfactory results thereafter.

In the accompanying table, the results thus far obtained with penicillin therapy are presented. In contrast to many investigators who used penicillin in combination with other therapeutic agents, e. g., heavy metals, arsenicals or fever, or injected

*Results of Treatment with Penicillin of 112 Patients with Neurosyphilis Followed Six Months or More*

| Diagnosis | Successful | Indefinite | Failure | Total |
|---|---|---|---|---|
| Asymptomatic type | 13 | 6 | 0 | 19 |
| Meningovascular type | 15 | 4 | 1 | 20 |
| Tabes dorsalis | 26 | 2 | 1 | 29 |
| Dementia paralytica | 26 | 2 | 0 | 28 |
| Tabetic form of dementia paralytica | 15 | 1 | 0 | 16 |
| Total no. | 95 | 15 | 2 | 112 |

it intravenously or intrathecally, we in Bellevue Hospital administered the drug exclusively by intramuscular injection. The only variations were in relation of time and dose. Some patients received a total of 2,000,000 units only, some 3,000,000 or 4,000,000 and a few even larger doses, the maximum dose so far given being 9,000,000 units. The time interval was three hours. The period of treatment lasted from nine to twenty-five days. All the patients were kept in the hospital during the entire course of treatment. The spinal fluid was examined before and after treatment, then every three months for a year and every six months thereafter. The longest period of observation was twenty months.

Only 112 patients are reported on here, although the number of treated patients exceeded 170. Only those patients who remained under observation at least six months are included in the statistical evaluation.

Forty-eight, almost one-half the patients, were under observation for more than a year. The outcome was considered indefinite when the spinal fluid syndrome showed a borderline cell count of 4 or 5 cells per cubic millimeter. However, we expect that some patients in the borderline group may finally be included with those for whom treatment was successful.

As can be seen from the table, the most favorable results were obtained with the so-called parenchymatous type of neurosyphilis. The reason for this paradoxic effect is that we gave only 2,000,000 units of penicillin in cases of asymptomatic and meningovascular syphilis. The failures, therefore, are to be attributed to the inadequate amount of penicillin, and they suggest that the amount of penicillin to be given should not depend on the clinical classification of the patient.

A few words about the effect of penicillin on the clinical manifestations of neurosyphilis: It is obvious that this question has no bearing on asymptomatic neurosyph-

ilis, since, by definition, asymptomatic neurosyphilis is syphilis of the central nervous system without signs and symptoms. Here, the spinal fluid findings are necessarily the only criterion of therapeutic success. Since asymptomatic neurosyphilis in pathoanatomic terms is meningovascular or parenchymatous neurosyphilis, we see no reason that we should change our point of view only because by chance the process has involved structures which give rise to clinical signs or symptoms. We are anxious to efface all clinical manifestations of the process. This, however, is rather a matter of luck than of the effectiveness of the therapeutic endeavor. To quote Vernes, the originator of the measurement of the serologic tests for syphilis, "We can't expect the water which put out the fire to repair the burned beams." It seems to us that the most common mistake is the failure to take into consideration that one is treating neither the signs nor the symptoms of the neurosyphilitic process, which reflects itself in the spinal fluid syndrome, but that one is trying to arrest the pathologic process, irrespective of what damage has already been done and whether it may or may not be reversible.

In summary, I may say, then, that thus far penicillin, when given in adequate doses, has proved to be at least as effective in the treatment of neurosyphilis as the combined fever and specific therapies. We still do not know what may be the optimal relationship of dose and time to obtain maximal therapeutic success.

DISCUSSION

Dr. H. Houston Merritt: We are fortunate in hearing this report, for, so far as I know, Dr. Dattner is the only person who is conducting a thorough study to determine the value of penicillin alone in the treatment of neurosyphilis. Most of the reports from the literature are confused by the fact that the workers combined penicillin treatment with fever therapy or chemotherapy. Dr. Dattner's studies will show what the exact value of penicillin is. All who have had experience in treating neurosyphilis are fervently hoping that penicillin will be the answer to their problem, because the methods of treatment used in the past, although moderately successful, were, to say the least, somewhat barbarous. Neurologists are greatly indebted to Wagner-Jauregg for the introduction of fever therapy, but it is not an ideal method. If a treatment can be found which is harmless to the patient and is as successful as, or more successful than, fever therapy, a great step forward will have been made. Dr. Dattner's report is encouraging, but it is too early to say that penicillin is the answer. It will be some time before it is known how much and how often penicillin must be given. The original idea that 2,000,000 or 3,000,000 units is sufficient will probably prove to be wrong, and it may be shown that 8,000,000 to 10,000,000 units will have to be given, perhaps two or three times, before the process is completely arrested.

I should also like to emphasize Dr. Dattner's statements regarding the results that can be obtained in the treatment of neurosyphilis. It cannot be expected that the treatment will restore dead tissue in the brain or the spinal cord; all that can be hoped for is that the treatment will arrest the process and that the natural reparative processes of the body will ameliorate some of the symptoms.

Dr. Leon H. Cornwall: I can only compliment Dr. Dattner on the study that he has made and the conservative manner in which he has arrived at his conclusions. I find that Dr. Merritt has touched a sensitive spot when he states that this is the only study of the sort that is being made. I am carrying out a similar investigation, and I am certain that many others are. I have nothing to criticize in Dr. Dattner's results or the way in which they have been presented. They accord with the small experience that I have had, but my material has not as yet been intensively studied. After all, the changes reported do not differ much from those obtained with the older methods of treatment except that they are more profound and that the clinical results occur more promptly. I cannot entirely agree with Dr. Merritt that all previous treatment has been barbarous. After all, a régimen of intramuscular injections every three hours is not very pleasant. I agree that penicillin therapy has definite advantages over fever therapy, which is certainly a

vigorous method, unsuitable for some patients, and not without dangers that do not obtain with penicillin. My feeling is not based on much information on the subject, but I think the time is not far off when it will be found that there are several factors in penicillin, as there are in the vitamin B complex. The future may reveal many interesting things regarding this extremely valuable preparation.

I note that Dr. Dattner has followed the newer methods used in some quarters for titrating colloidal gold, the reaction of the spinal fluid and the serologic reactions of the blood. From my observation, I have not yet been much impressed with the significance of these titrations. I think that unwarranted interpretations have been made. This opinion may be due to insufficient familiarity with the technics. I made a rather naughty remark once concerning an article that appeared several months ago regarding the significance of colloidal gold reactions. The article appeared to imply that one can make a diagnosis of dementia paralytica from the colloidal gold curve alone. My impression is that one makes this diagnosis from clinical observations and that certain laboratory findings help to confirm it. The naughty remark was that if I had been the editor and had been titling the article, I should have used the caption, "Much Ado about Nothing," and I should have made just one conclusion, "So what?" In saying that, I do not mean to imply any criticism of Dr. Dattner's observations. They have been well presented, and I find nothing with which to disagree.

DR. H. A. RILEY: Has Dr. Dattner any opinion regarding the value of combined malaria and penicillin treatment?

DR. IRVING PARDEE: Has Dr. Dattner had any untoward reactions?

DR. BERNHARD DATTNER: I wish to thank Dr. Merritt for his favorable comments. Being associated with his service, I know that we agree in essential points regarding the diagnosis and treatment of neurosyphilis. I must side with him against Dr. Cornwall that the methods used before the advent of penicillin therapy were medieval in character. Although I have been working with malarial therapy from its inception, I should not hesitate for one moment to replace it with penicillin therapy. Treatment with tryparsamide must be considered also as a strenuous form of therapy, for injections must be continued a long time, sometimes for years. Treatment by injections of penicillin, even when given every three hours, compares favorably with it, because it lasts two or three weeks only. We are at present investigating the therapeutic effect of a single daily injection of 300,000 units of penicillin in beeswax and peanut oil. I am quite sure that in the near future we may obtain an equally good effect with one weekly injection of highly concentrated penicillin.

We were at the beginning equally inclined to pay little attention to the modified colloidal gold curve of Lange. However, when numerical values are given to the Wassermann reagins and the proteins, it makes it easier to show the trend of the results by comparing the relative figures for all the tests. The high sensitivity of the colloidal gold curve gives additional information about the nature of the pathologic process. Since dementia paralytica invariably shows a first zone type of curve, the finding of the same type of curve in a case of asymptomatic neurosyphilis is of serious portent. It is no wonder that a patient with asymptomatic neurosyphilis and a first zone type of colloidal gold curve proves overnight to have dementia paralytica.

We were giving penicillin in doses of 30,000 and 40,000 units every three hours.

In reply to Dr. Riley, I wish to stress again that we abstained from combining penicillin with fever in order to gain information on the pure effect of penicillin. Since we know that we shall never have therapeutic success of 100 per cent, it may well be advisable to combine fever with penicillin in treatment of the patient with the refractory condition.

We had only one allergic reaction, which forced us to discontinue treatment of a patient with syphilitic myelitis and disturbances of bladder control. Urticaria, fever and general malaise developed. Otherwise, we had no untoward response.

**Myelination of the Central Nervous System of Natrix Sipedon.**
Dr. Francis James Warner, Chicago (by invitation).

Myelination occurs first in the cervical region of the spinal cord of Natrix sipedon. The medial longitudinal bundle and the lateral vestibulospinal tract are the first tracts to become medullated at the cervical level of the spinal cord. The fasciculus cuneatus is medullated earlier than the fasciculus gracilis. The spinocerebellar and the spinomesencephalic tract are medullated in the spinal cord later than the descending tracts.

In the brain stem, the medial longitudinal bundle, the vestibular nerve and the lateral vestibulospinal tract become medullated early. The dorsal tectobulbar tracts medullate sooner than the ventral tectobulbar tract. The vestibulocerebellar and the spinocerebellar tract do not reach the cerebellum until a fairly late stage (213 mm.). The lateral lemniscus is medullated and can be traced to the inferior corpora quadrigemina at the 188 mm. stage. The cochlear root of the eighth cranial nerve medullates earlier in this snake than in the opossum or the cat (at the 163 mm. stage in Natrix sipedon). The optic tracts and the optic layer of the optic tectum do not become medullated until a rather late stage (238 mm.).

The fiber tracts of the spinal cord, medulla and midbrain in Natrix sipedon medullate in an order similar to that in the cat, as noted by Tilney and Casamajor (1924), and Langworthy (1929) and also to that of the opossum, as described by Langworthy (1928). Thus, in Natrix sipedon, as in marsupials and mammals, the most ancient fiber tracts phylogenetically medullate earlier than the fiber tracts of recent development.

DISCUSSION

Dr. Otto Marburg: The excellent investigations of Dr. Warner on the snake are also of great importance for our studies of the pathways in man. The simple relations in so low an animal make it possible to recognize the rather complicated relations in man. This is easily seen with the posterior longitudinal system (medial longitudinal bundle), the connection of which with the vestibular centers is distinctly recognizable. It is surprising how well developed this system of primitive orientation in space is in snakes. On the contrary, the red nucleus and its pathways are scarcely developed, an indication of underdevelopment of the mechanisms for the orientation of the body itself. That alone is evidence for the importance of these studies.

# Book Reviews

**Manual of Diagnostic Psychological Testing. Volume II: Diagnostic Testing of Personality and Ideational Content.** By David Rapaport and Roy Schafer. With the Collaboration of Merton Gill. Price, $0.75. Pp. 100. New York: Josiah Macy Jr. Foundation, 1946, Review Series, Volume III, No. 1.

In volume II the authors pursue the systematic exploration of the diagnostic values of widely used psychologic tests. Under discussion are the Rorschach, the Thematic Apperception and the Word Association Test, elaborately analyzed from the point of view of their rationale as personality evaluators, their clinical application and their statistical validation as diagnostic indicators.

The clinical data were obtained from 217 psychiatric patients, schizophrenia, paranoid reactions, depressions and neuroses being represented. Organic and psychopathic personality entities were not included. As the control, a group of 54 "normal" subjects were selected from the Kansas highway patrol.

To be highly commended is the approach to the formulation of a consistent theory of personality revelation through projective technics, the general projective hypothesis being "that the person's behavior manifestations—including the least and most significant or deviant—are revealing of his personality." This discussion (covered largely in the introductory passages) should prove of interest to both the psychiatrist and the psychologist.

For the clinical psychologist, there is a wealth of specific aid in areas such as the differential diagnosis of groups and subgroups; the precise management of difficulties to be encountered with psychiatric patients; the concrete proposals for positive utilization of negative aspects of the Thematic Apperception Test, such as disguised refusal, and the revision of the Word Association Test to point up areas of conflict.

So many diverse psychologic types have been included under the general classification of schizophrenic disorders that the authors' suggestion of differentiation into a hierarchy of malignancy with reference to findings in psychologic tests is particularly welcome.

After an introductory passage, lauding the simplicity and ease of Rorschach's original scoring, it is difficult to accept the many complex elaborations and refinements then offered by the authors. In view of the already existing variations in scoring, the burden of proof for further changes must fall heavily on the new advocates. While one may be in full accord with the statement that "the Rorschach is the most potent psychological test extant," it is refreshing to find an evaluation of the limitations of this technic (as with paranoid conditions), with positive recommendations for overcoming such lacks through a supplementary battery.

Although the statistical validation is still on an insecure foundation, the wealth of empiric experience and observation is impressive and provocative. This book is highly recommended.

**Introduction to Clinical Neurology.** By Gordon Holmes, M.D., F.R.S. Price, $4. Pp. VII, plus 183. Baltimore: Williams & Wilkins Company, 1946.

Dr. Gordon Holmes has presented in this small volume the essence of his teaching at the National Hospital for Nervous Diseases. The book is not intended to take the place of standard textbooks of neurology. Rather than present original research, a review of the literature or case reports, he offers a survey of the field suitable for medical students. It is valuable, because in a few hours' reading one gets a well proportioned discussion of the subject. Disease syndromes are not described, nor are authors and journals cited. The plan of the book is a systematic and beautifully orderly discussion of the functional anatomy and the normal and abnormal physiology of the nervous system, as well as of the clinical methods used in its study.

Dr. Holmes begins with a general discussion of the importance of nervous symptoms and signs, a very brief chapter on the major classes of nervous lesions

and a chapter on the systematic examination of the patient. Succeeding chapters are devoted to the motor systems, muscle tone and its maintenance, and involuntary movements; sensation and its examination; reflexes; vision and ocular movements; postural reactions and the vestibular system; speech, agnosia and apraxia; excretory and autonomic regulation, and the patient's mental state. Each section describes the normal function, the nature of its disorders, with their signs and symptoms, and the tests used in detection of these.

Like many British medical works, this book is particularly well written. Far more detailed information is actually presented than may appear at first glance. Recent developments in such fields as electroencephalography and the study of agnosia and body image are not neglected. The chapters on complex nervous functions, such as speech and ocular movements, always difficult to present clearly, are particularly good. The author carefully prefers descriptive terms, such as "plantar reflex," to eponymous ones. No illustrations are given except a few line drawings and diagrams.

While primarily of value to the beginning student of neurology, this introduction should be examined with interest by all who care to observe the arrangement, the emphasis and the selection of material employed by this great modern neurologist in reviewing his field.

**Insight and Personality Adjustment.** By Therese Benedek, M.D. Price, $4. New York: The Ronald Press Co., 1946.

"Love is the goal of human nature and, individually as well as within a nation and among nations, it can be attained only by a complex process of maturation." Dr. Benedek states this in her study of the psychologic effects of war and then proceeds to describe this maturation.

The normal development of various kinds of interpersonal relationships and their disturbance by war form the foundation on which her book is built. Freudian concepts brought up to date and modified by Dr. Benedek are used for the framework. War literature and sketchy fragments of case histories constitute the bricks of the building.

Since children, adolescents, soldiers, their wives and their parents have been affected by war, almost all personality problems created by war are within the scope of the book. Much space is devoted to the differences between masculinity and femininity and to disturbances in their development. It is implied that mature masculinity is characterized by activity, independence, dominance and mastery over the female and that dependence on, or even equality with, the female signifies immaturity or regression. However, this seems questionable, since one sign of a mature adult relationship is marriage, which is based on an acceptance of the interdependence of the sexes.

This book was written for social workers, clergymen, teachers, counselors, psychologists, physicians and psychiatrists. Because of the variety of people for whom it is written, it may seem trite to some and too technical to others. Even though it may give only partial insight, it sheds light on many personality problems created by the war.

**Human Embryology.** By Bradley M. Patten. Price, $7. Pp. 776. Philadelphia: The Blakiston Company, 1946.

This new and important textbook is a valuable contribution to medical teaching. Emphasis is given to those aspects of embryology which are of importance as a background of other medical subjects. Functional aspects are well correlated with development, making for greater interest and usefulness. In the chapters dealing with each of the systems, the developmental data are oriented toward practical medicine, and each chapter ends with a discussion of the more common anomalies.

The style of writing is simple and clear; the photographs and drawings are profuse in number and excellent in quality.

This volume should be invaluable not only to medical students, but also to practitioners interested in the embryonic basis of developmental anomalies.